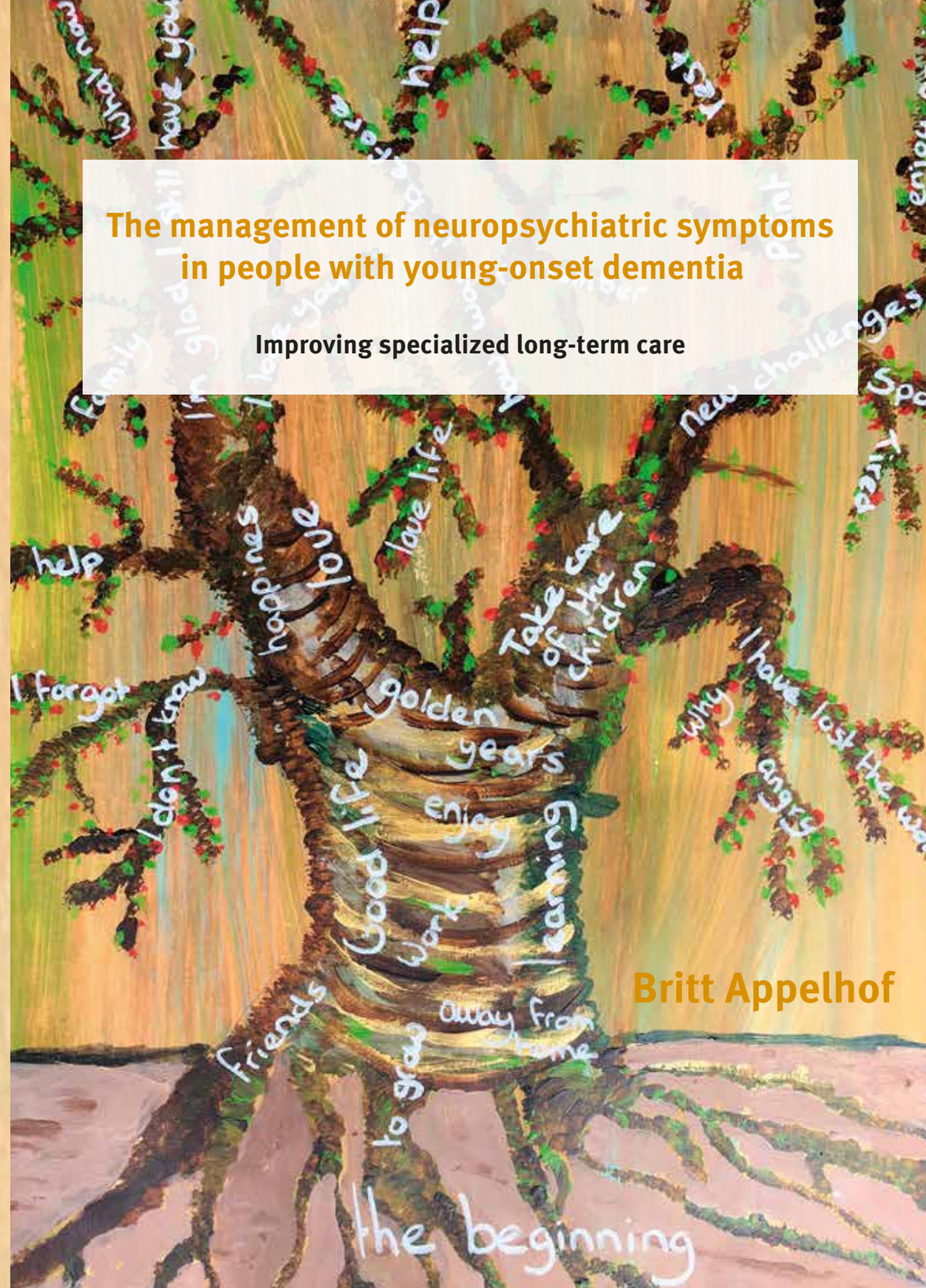
Britt Appelhof The management of neuropsychiatric symptoms in people with young-onset dementia



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Improving specialized long-term care

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Chapter 1

GENERAL INTRODUCTION

This thesis is part of the Behavior and Evolution of Young ONset Dementia part 2 (BEYOND-II) study. In this study a multi-component intervention for the management of neuropsychiatric symptoms (NPS) in nursing home (NH) residents with young-onset dementia was developed and implemented in special care units for people with young-onset dementia.

Young-onset dementia: definition, prevalence, and etiology

Although dementia is considered a disease of old age, in some people first symptoms already develop before the age of 65. There is no consensus on the nomenclature concerning these younger people with dementia [1]. In the current literature, most commonly the term young-onset dementia (YOD) is used [2]. However, confusingly also presenile dementia, early onset dementia, and younger onset dementia are often used [1]. Besides discussion on the nomenclature, also the cut-off at age 65 is considered arbitrary. This cut-off age is related to the social division in terms of employment and retirement age. However, younger people with dementia also differ from older individuals with dementia on biological factors (e.g. genetics, hereditary patterns, etiology, comorbidities, course of the illness, clinical presentation) and other social characteristics (e.g. vitality, social network, family structure, day time activities) [1, 3-7].

No studies on the prevalence of YOD in the Netherlands have been conducted, although these estimates are critical for policymaking and care planning. International studies on the prevalence of YOD are scarce. Furthermore, prevalence rates in these studies are likely an underestimation as they are based on people who had contact with health care services. However, not all people with dementia will seek help early in the course of the disease [8]. In the UK the prevalence of YOD was estimated 54.0 per 100,000 [9]. A more recent Australian study estimated a higher prevalence of 68.2 per 100,000 [10]. When applying these percentages found in the UK and Australia to the Dutch population, this would indicate a prevalence between 9,000 and 11,000 individuals with YOD in the Netherlands. More research with larger sample sizes is needed to allow for estimates with more precision [8].

There is a large variation in the prevalence estimates of the different causes of YOD between studies. Overall, Alzheimer's dementia (AD), as in late-onset dementia (LOD), is the most prevalent cause in younger individuals [11]. Nonetheless, the etiology of dementia in younger people is more heterogenic: higher proportions of less common causes of dementia like frontotemporal dementia (FTD) and alcohol-related dementia have been found [10, 11]. Furthermore, in the youngest individuals, with a disease onset before the age of 45 years, it is more likely that a genetic or metabolic disease is causing the dementia [11].

Long-term care in young-onset dementia

Most people with dementia eventually are admitted to NHs. The time from symptom onset to institutionalization is more than twice as long for people with YOD (mean 9 years) compared to people with LOD (mean 4 years) [12]. This might be related to better physical health of the caregivers of younger people with dementia [12]. Also, the limited availability of age-appropriate residential care facilities, differences in progression of YOD, and the stigma attached to dementia might be explanations [13].

To improve quality of care for people with YOD and their families the Dutch YOD Knowledge Center (DKC) was founded in 2001. Currently thirty health care organizations as well as several academic centers, general hospitals, and foundations for dementia (e.g. FTD lotgenoten, Alzheimer Nederland, Deltaplan dementie) have joined the DKC. The DKC develops specific guidelines for YOD, supports scientific research, provides education for health care professionals, and promotes the implementation of research findings in clinical practice. All affiliated health care organizations provide dedicated YOD services, including specialized long-term care units (SCU's) for people with YOD. In the Netherlands, similar to residential care units for elderly people with dementia, care at YOD SCU's is provided by a multidisciplinary team. This multidisciplinary team consists of at least nursing staff, psychologist, paramedic disciplines (e.g. physical therapist, speech therapist, occupational therapist, dietician) and elderly care physicians [14, 15]. All disciplines are employed by the NH, in contrast to most other countries in which these disciplines are not always available or only available through consultation of other healthcare organizations [15].

Prevalence and management of neuropsychiatric symptoms in young-onset dementia

In the care for NH residents with YOD, high prevalence rates of NPS pose a challenge [16]. NPS are defined as every form of behavior that results in reduced wellbeing of the resident or is considered dangerous for either the residents themselves or others in their surroundings, like nursing staff members, clinicians, relatives, or other residents [17]. NPS encompass various symptoms such as depression, anxiety, apathy, aggression, agitation, disinhibition, delusions, and hallucinations. Mulders et al. (2016) found that NPS occurred in almost all NH residents with YOD, with agitation (88%) and apathy (56%) being the most prevalent symptoms [16]. Those prevalence rates of NPS seem higher compared to those in LOD NH residents [18]. However, the few studies that directly compared rates of NPS between young-onset AD and late-onset AD in the community-dwelling population suggest less NPS in people with young-onset AD [19-21]. Studies directly comparing NPS in heterogeneous samples of NH residents with YOD and LOD are still lacking. Research on NH residents with

LOD has shown that NPS are associated with negative health outcomes for the person with dementia as well as for health care professionals, such as a loss of quality of life, increased cost of care, and high workload for the NH staff [22-24]. These negative health outcomes are likely to also apply to YOD. Indeed, van Duinen-van den IJssel et al. (2017) found that nursing staff distress is related to NPS in NH residents with YOD [25]. However, to our knowledge no studies on other consequences of NPS in residents with YOD have been conducted. Psychotropic drugs are often used in the treatment of NPS in dementia, and especially in institutionalized people with YOD. Mulders et al. (2016) showed that 87 percent used one or more psychotropic drug(s) [16]. Studies on the effect of psychotropic drug treatment on NPS in YOD have not yet been performed. Nonetheless, psychotropic drugs have been associated with poor health outcomes (like stroke, increased mortality) and reduced quality of life in NH residents with LOD [23, 26, 27].

The high prevalence rates of NPS and psychotropic drug use (PDU) in YOD stresses the importance of successful management of NPS in YOD, in which psychotropic drugs are only prescribed if other treatment options have little or no effect. In order to successful manage NPS, the underlying causes of NPS needs to be resolved and treated. Cohen-Mansfield developed the unmet-needs framework [28], in which NPS are perceived as behaviors through which the person with dementia might indirectly communicate an underlying need. Because of cognitive and functional decline, the person with dementia is less able to address and also communicate these needs. These needs can be medical (e.g. physical illness, pain, mobility), psychosocial (e.g. life habits, premorbid personality), or environmental (e.g. under/over stimulation, behavior of NH staff or other residents) [29, 30]. Although specific facilities for younger people with dementia are provided in the Netherlands, most services are designed for older people and might not always be well equipped to address the specific needs of younger individuals, for instance regarding daytime activities, social interaction, mobility, and intimate relationships [6]. Therefore, people with YOD might be at particular risk for developing unmet care needs.

An intervention for the multidisciplinary team that offers a systematic approach in the treatment of NPS taking into account the specific needs of younger individuals is lacking. Therefore, in the BEYOND-II study a multi-component intervention which has shown effectiveness in the management of NPS in older people with dementia (Grip on challenging behavior care program), was adapted to the specific characteristics of NH residents with YOD [31, 32]. This intervention provided guidance for the multidisciplinary team involved in the management of NPS in NHs (nursing staff, specially trained elderly care physicians and psychologists) to structure the process of detection, analysis, treatment,

and evaluation of NPS. In order to address unmet care needs and the high prevalence rates of PDU in NH residents with YOD, a tool for the detection of unmet needs [33] and a tool for the evaluation of appropriateness of psychotropic drug prescription were [34] added to the original intervention. Also an enhanced implementation strategy was designed, based on existing knowledge about the implementation of complex interventions in long-term care to facilitate implementation in the thirteen participating YOD special care units.

Implementation of interventions in nursing homes

When implementing an intervention in the context of daily practice, researchers are often faced with practical difficulties [35]. Contextual factors external to the intervention (like staff turnover, organizational changes, staff motivation) could facilitate or hinder implementation [36, 37]. Indeed, intervention studies in NHs are often faced with variation in adherence of parts of the intervention [38-41]. Potentially effective interventions may fail to show effectiveness due to limited implementation. To understand why the intervention for the management of NPS in NH residents with YOD was or was not effective, it is important to get insight into the degree of implementation and contextual factors influencing implementation. Furthermore, reporting on the implementation strategy and how it was received provides future users of the intervention with vital information about how to reproduce the intervention.

Aims and outline of the thesis

This thesis is part of the BEYOND-II study. Focus of this thesis is on differences in NPS between residents with YOD and LOD, and the consequences of NPS for the quality of life of residents with YOD in order to further improve specialized long-term care for younger individuals. In addition, the implementation process and effects of a multi-component intervention for the management of NPS in institutionalized people with YOD were evaluated.

The following research questions were addressed:

1. *What are the determinants of quality of life of NH residents with YOD and are there differences between dementia subtypes regarding these determinants?*
   NPS and PDU are associated with a loss of quality of life of NH residents with LOD. This negative influence is expected to also apply to YOD, although this has not yet been investigated. Insight into the determinants that influence quality of life is necessary to improve care and well-being of residents with YOD (Chapter 2).

2. *Are there differences in NPS between NH residents with YOD and LOD, and can these possible differences be attributed to differences in dementia subtype, gender, psychotropic drug use, or dementia severity?*
   The results of the few studies directly comparing NPS between YOD and LOD are inconsistent. In addition, in these studies only people with AD were involved and the possible influence of PDU was not taken into account.
   To develop more effective treatments and further enhance NH care for residents with YOD, it is important to gain more insight into differences in NPS between heterogeneous samples of NH residents with YOD and LOD and the specific characteristics of YOD that might contribute to these possible differences (Chapter 3).

3. *Are internal and external validity of a multi-component intervention study on the management of NPS in NH residents with YOD sufficient and what are barriers and facilitators for implementation of the intervention?*
   To interpret the effects of the intervention for the management of NPS in YOD (Chapter 4), information on validity and degree of implementation is important. Furthermore, implementation knowledge is important to optimize implementation strategies for future complex interventions in applied NH care. A process evaluation which provides knowledge on validity and implementation was performed before the effect analysis (Chapter 5).

4. *What is the effect of a multi-component intervention on the prevalence of NPS (particularly agitation and aggression) and PDU in residents with YOD compared to care as usual?*
   In order to evaluate effectiveness, the intervention for the management of NPS in YOD was implemented on thirteen YOD SCUs. A randomized controlled trial was conducted using a stepped wedge design (Chapter 6).

References

1. Koopmans R, Rosness T: Young onset dementia-what does the name imply? International Psychogeriatrics 2014;26(12):1931-1933.
2. Draper B, Withall A: Young onset dementia. Internal Medicine Journal 2015;46(7):779-786.
3. Koedam ELGE, Lauffer V, van der Vlies AE, et al.: Early-versus late-onset Alzheimer's disease: more than age alone. Journal of Alzheimer's Disease 2010;19(4):1401-1408.
4. Gerritsen AEJ, Bakker C, Verhey FRJ, et al.: Prevalence of Comorbidity in Patients With Young-Onset Alzheimer Disease Compared With Late-Onset: A Comparative Cohort Study. Journal of the American Medical Directors Association 2016;17(4):318 323.
5. Harris PB, Keady J: Selfhood in younger onset dementia: Transitions and testimonies. Aging & Mental Health 2009;13(3):437-444.
6. Bakker C, de Vugt ME, van Vliet D, et al.: The relationship between unmet care needs in young-onset dementia and the course of neuropsychiatric symptomps: a two year follow-up study. International Psychogeriatrics 2014;26(12):1991–2000.
7. Rossor MN, Fox NC, Mummery CJ, Schott JM, Warren JD: The diagnosis of young onset dementia. The Lancet Neurology 2010;9(8):793-806.
8. World Health Organization: Dementia: A Public Health Priority, World Health Organization, 2012.
9. Harvey RJM, Skelton-Robinson M, Rossor MN: The prevalence and causes of dementia in people under the age of 65 years. Journal of neurology, neurosurgery, and psychiatry 2003;74(9):1206-1209.
10. Withall A, Draper B, Seeher K, Brodaty H: The prevalence and causes of younger onset dementia in Eastern Sydney, Australia. International Psychogeriatrics 2014; 26(12):1955-1965.
11. Vieira RT, Caixetal L, Machado S, et al.: Epidemiology of early-onset dementia: a review of the literature. Clinical Practice & Epidemiology in Mental Health 2013;9: 88-95.
12. Bakker C, de Vugt ME, van Vliet D, et al.: Predictors of the time to institutionalization in young-versus late-onset dementia: results from the needs in young onset dementia (NeedYD) study. Journal of the American Medical Directors Association 2012;14: 248–253.
13. Bakker C, de Vugt ME, van Vliet D, et al.: The use of formal and informal care in early onset dementia: results from the NeedYD study. The American journal of

geriatric psychiatry: official journal of the American Association for Geriatric Psychiatry 2013;21(1):37-45.

14. Koopmans RCTM, Pellegrom M, van der Geer ER: The Dutch Move Beyond the Concept of Nursing Home Physician Specialists. Journal of the American Medical Directors Association 2017;Epub ahead of print.

15. Ribbe MW, Ljunggren G, Steel K, et al.: Nursing homes in 10 nations: a comparison between countries and settings. Age and Ageing 1997;26:3-12.

16. Mulders AJMJ, Fick IWF, Bor H, et al.: Prevalence and correlates of neuropsychiatric symptoms in nursing home patients with young-onset Dementia: The BEYOnD Study. Journal of the American Medical Directors Association 2016;17(6):495-500.

17. Verenso: Richtlijn Probleemgedrag bij mensen met dementie, Verenso, 2018.

18. Selbæk G, Engedal K, Bergh S: The prevalence and course of neuropsychiatric symptoms in nursing home patients with dementia: a systematic review. Journal of the American Medical Directors Association 2013;14(3):161-169.

19. Mushtaq RA, Pinto C, Tarfarosh SFA, et al.: Comparison of the Behavioral and Psychological Symptoms of Dementia (BPSD) in Early-Onset and Late-Onset Alzheimer's Disease - A Study from South East Asia (Kashmir, India). Cureus 2016; 8(5):e625.

20. Toyota Y, Ikeda M, Shinagawa S, et al.: Comparison of behavioral and psychological symptoms in early-onset and late-onset Alzheimer's disease. International Journal of Geriatric Psychiatry 2007;22(9):896-901.

21. van Vliet D, de Vugt ME, Aalten P, et al.: Prevalence of neuropsychiatric symptoms in young-onset compared to late-onset Alzheimer's disease - part 1: findings of the two year longitudinal NeedYD-study. Dementia and Geriatric Cognitive Disorders 2012; 34(5-6):319-327.

22. Murman DL, Chen Q, Powell MC, et al.: The incremental direct costs associated with behavioral symptoms in AD. Neurology 2002; 59(11):1721-1729.

23. Wetzels R, Zuidema SU, de Jonghe J, et al.: Determinants of quality of life in nursing home residents with dementia. Dement Geriatr Cogn Disord 2010;29(3):189-197.

24. Zwijsen SA, Kabboord A, Eefsting JA, et al.: Nurses in distress? An explorative study into the relation between distress and individual neuropsychiatric symptoms of people with dementia in nursing homes. International Journal of Geriatric Psychiatry 2014;29(4):384-91.

25. van Duinen-van den IJssel JCM, Mulders AJMJ, Smalbrugge M, et al.: Nursing Staff Distress Associated With Neuropsychiatric Symptoms in Young-Onset Dementia and

Late-Onset Dementia. Journal of the American Medical Directors Association 2017; Epub ahead of print.

26. Ballard C, Howard R: Neuroleptic drugs in dementia: benefits and harm. Nature Reviews Neuroscience 2006;7(6):492-500.

27. Schneider LS, Dagerman K, Insel PS: Efficacy and adverse effects of atypical antipsychotics for dementia: meta-analysis of randomized, placebo-controlled trials. American Journal of Geriatric Psychiatry 2006;14(3):191-210.

28. Cohen-Mansfield J: Use of Patient Characteristics to Determine Nonpharmacologic Interventions for Behavioral and Psychological Symptoms of Dementia. International Psychogeriatrics 2010;12:373-380.

29. Cohen-Mansfield J: Heterogeneity in dementia: challenges and opportunities. Alzheimer Disease and Associated Disorders 2000;14(2):60-63.

30. Cohen-Mansfield J, Billig N: Agitated behaviors in the elderly. A conceptual review. Journal of the American Geriatrics Society 1986;34:711–721.

31. Zwijsen SA, Smalbrugge M, Eefsting J, et al.: Coming to grips with challenging behavior: a cluster randomized controlled trial on the effects of a multidisciplinary care program for challenging behavior in dementia. Journal of the American Medical Directors Association 2014;15(7):531.e1-531.e10.

32. Zwijsen SA, Smalbrugge M, Zuidema SU, et al.: Grip on challenging behaviour: a multidisciplinary care programme for managing behavioural problems in nursing home residents with dementia. Study protocol. BMC Health Services Research 2011;11(41): 1-6.

33. Orrell M, Hancock G: CANE: Camberwell Assessment of Need for the Elderly, Gaskell, 2004.

34. van der Spek K, Gerritsen DL, Smalbrugge M, et al.: A reliable and valid index was developed to measure appropriate psychotropic drug use in dementia. Journal of Clinical Epidemiology 2015;68(8):903-912.

35. Vernooij-Dassen M, Moniz-Cook E: Raising the standard of applied dementia care research: addressing the implementation error. Aging and Mental Health 2014;18(7):809-814.

36. Moore G, Audrey S, Barker M, et al.: Process evaluation of complex interventions: Medical Research Council guidance. BMJ 2015;350: 1-7.

37. Peters DH, Taghreed A, Agyepon A, Alonge O, Tran N: Implementation research: what it is and how to do it. BMJ 2013;347:1-7.

38. Pieper MJC, van der Steen JT, Francke AL, et al.: Effects on pain of a stepwise

multidisciplinary intervention (STA OP!) that targets pain and behavior in advanced dementia: A cluster randomized controlled trial. Palliative Medicine 2018;32(3):682 692.

39. van de Ven G, Draskovic I, Adang EMM, et al.: Effects of dementia-care mapping on residents and staff of care homes: a pragmatic cluster-randomised controlled trial. PLoS One 2013;8(7):1-7.

40. Zwijsen SA, Smalbrugge M, Eefsting JA, et al.: Grip on challenging behavior: process evaluation of the implementation of a care program. Trialsjournals 2014;15:2-11.

41. Ruikes FGH, van Gaal BGI, Zuidema SU, et al.: The association between implementation and outcome of a complex care program for frail elderly people. Family Practice 2018;35(1):47-52.

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Chapter 2

QUALITY OF LIFE OF NURSING HOME RESIDENTS WITH YOUNG-ONSET DEMENTIA

The determinants of quality of life of nursing home residents with young-onset dementia and the differences between dementia subtypes

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Abstract

Aims: The aims of this study are to (1) explore the determinants of quality of life (QoL) in nursing home residents with young-onset dementia (YOD), (2) investigate whether there are differences between dementia subtypes (Alzheimer's dementia, vascular/mixed dementia, frontotemporal dementia, other) regarding these determinants, and (3) compare QoL profiles of YOD nursing home residents across dementia subtypes.
Methods: This cross-sectional study included 207 nursing home residents. Multilevel modeling was used to determine the relationships between QoL and neuropsychiatric symptoms (NPS), dementia severity, psychotropic drug use (PDU), dementia subtype, age, and gender. Additional multilevel models were used to compare aspects of QoL between dementia subtypes.
Results: Residents' QoL was negatively associated with advanced dementia, PDU, and NPS. In general, the relationships between the determinants and QoL were similar across the dementia subtypes. Aspects of QoL differed by dementia subtype. Residents with FTD showed less negative emotions, accepted more help and experienced better quality of relationships with professional caregivers, had a more positive self-image, felt more comfortable in the nursing home environment, and experienced lower quality of social relationships.
Conclusions: Considering the high rates of NPS and PDU in YOD residents and their negative associations with QoL, we recommend emphasizing services to manage and reduce NPS and PDU in nursing home residents with YOD. Furthermore, our findings suggest accounting for differences in aspects of QoL by dementia subtype to address specific needs and thereby improve QoL.

Introduction

Quality of life (QoL) is increasingly recognized as an important measure of general well-being in dementia [1]. Therefore, in the past decade, several studies have investigated the factors that influence QoL in people with dementia. Better QoL has been associated with a reduced awareness of people's own cognitive deficits and better mental health of the caregiver in community-dwelling people with dementia [2,3]. Additionally, the subtype of dementia might be associated with QoL. For instance, Bostrom et al. (2007) and Thomas et al. (2006) found a significant lower QoL in community-dwelling people with Lewy body dementia (LBD) compared to Alzheimer's dementia (AD) [3,4]. Furthermore, increased cognitive impairment and the presence of neuropsychiatric symptoms (NPS) were negatively associated with QoL in both community-dwelling people and nursing home residents with dementia [2,3,5-13]. Of the NPS studied, especially depression was strongly associated with lower scores of QoL [5,7-11,14-16]. In addition, apathy, psychosis and agitation are negatively associated with QoL [7,10,17]. Moreover, NPS are often treated with psychotropic drugs, some of which have also been associated with poor health outcomes and reduced QoL in nursing home residents with dementia [5,7,18].

The current knowledge on the determinants of QoL in dementia is largely based on research with people with late-onset dementia (LOD). People with young-onset dementia (YOD), defined as dementia with an onset of symptoms before the age of 65 years, often encounter specific challenges such as a substantial delay in diagnosis, loss of employment, financial issues, social isolation, changes in relationships, and lack of meaningful daytime activities, all adding to the negative impact on QoL [19-22]. Indeed, current research suggests that younger age is associated with a worse QoL in LOD [9]. Furthermore, NPS are very common in nursing home residents with YOD. A recent Dutch study showed that 90% of nursing home residents with YOD showed one or more NPS [24,25]. Of the residents, 87% used one or more psychotropic drug(s) [24]. These prevalence rates of NPS and psychotropic drug use (PDU) seem even higher than in LOD [24,25], placing younger nursing home residents with dementia at particular risk of experiencing poor QoL.

Research on the determinants of QoL in YOD is scarce. One Dutch study found that lower levels of QoL in community-dwelling people with YOD were associated with higher levels of depression [26]. In that study, no association was found between QoL and other NPS or dementia severity. A recent review noted that the studies on QoL in YOD are heterogeneous in terms of the included dementia subtypes, which may have a negative impact on the consistency of the results [27]. The authors suggest that studies should

include homogeneous samples to improve the understanding of the determinants of QoL in YOD. Moreover, in current research on YOD, unclear definitions of the concept of QoL are used, and therefore it is uncertain which specific aspects of QoL were measured [27]. The multidimensionality of the QoL construct stresses the importance of investigating QoL domains separately to provide clarity regarding the possible differences in specific QoL domains and thereby prevent a loss of information [28-30]

A better understanding of the determinants of QoL in YOD and the possible differences in QoL across dementia subtypes can improve the care of YOD nursing home residents. Therefore, the aims of the current study are to (1) explore the determinants (NPS, PDU, dementia subtype, dementia severity, age, gender) of QoL in YOD nursing home residents, (2) investigate whether there are differences between dementia subtypes regarding the determinants of QoL, and (3) compare the QoL domains of residents across the three most common YOD subtypes.

Materials and methods

Study design and selection of participants

In this cross-sectional study, baseline data from a larger multicenter study aimed at the improvement of the management of challenging behavior in YOD, the Behavior and Evolution of Young-ONset Dementia part 2 (BEYOND-II) study, were used. Thirteen YOD special care units (SCUs) were recruited through nursing homes that are affiliated with the Dutch YOD Knowledge Center (DKC). Residents with a dementia diagnosis with a symptom onset before the age of 65 who resided on the SCU for at least one month were eligible for inclusion in the study. The exclusion criteria were lack of informed consent, dementia caused by human immunodeficiency virus (HIV), traumatic brain injury, Down's syndrome, Korsakov syndrome or Huntington's disease. The dementia diagnosis was established according to the 4th edition of the Diagnostic and Statistical Manual of Mental Disorders, text revision 2000 and international accepted criteria for diagnosing dementia subtypes were used and were retrieved from medical files [31-36].

The study protocol was approved by the Medical Ethics Committee region Arnhem/Nijmegen (file number 2015-1558) and registered in the Dutch Trial Register (Trial ID NTR5018). This research project was conducted according to the principles of the Declaration of Helsinki (version November 2013, www.wma.net) and in agreement with the laws regarding medical-scientific research in humans (WMO).

Data collection and assessments

Information on in- and exclusion criteria was sent to the participating SCUs for the initial selection of residents eligible for the study. The legal representatives of the residents who met inclusion criteria were asked for written informed consent. All data were anonymized. Trained researchers and research assistants collected the data through structured interviews with the nursing staff and from the resident's medical files. Regular consensus meetings with the research team ensured the integrity of the data collection process.

Quality of life

Quality of life (QOL) was assessed with the Quality of Life in Dementia (Qualidem) questionnaire. The Qualidem is an observational instrument and the reliability and validity are satisfactory [11,28]. The scale includes 37 items describing observable behavior with four possible responses to how often this behavior has been observed in the past week, ranging from never to almost daily. The Qualidem consists of nine subscales: Care relationship (ranging from 0 – 21), Positive affect (ranging from 0 – 18), Negative affect (ranging from 0 – 9), Restless tense behavior (ranging from 0 – 9), Positive self-image (ranging from 0 – 9), Social relations (ranging from 0 – 18), Social isolation (ranging from 0 – 9), Feeling at home (ranging from 0 – 12), and Having something to do (ranging from 0 – 6). A total score is calculated by summing the scores of the nine subscales (ranging from 0-111). Higher (sub) scale scores indicate a higher QoL.

Other resident characteristics

NPS were assessed using the Dutch version of the Neuropsychiatric Inventory-nursing home version (NPI-NH). The NPI-NH has a high-interrater reliability and has been found to be a valid instrument for the assessment of a wide range of NPS in dementia [37,38]. For each symptom, the Frequency (F) and Severity (S) are rated on a four-point (ranging from 1-4) and three-point scale (ranging from 1-3). We used NPI-NH factor scores based on a previous study in which five NPI-NH factors in a large nursing home sample were found: (1) agitation/ aggression, (2) depression (3) psychosis (4) psychomotor agitation and (5) apathy [39].

Dementia severity was assessed with the Global Deterioration rating Scale (GDS) [40]. The GDS is a validated scale that describes seven different stages of dementia ranging from "subjectively and objectively normal cognition" to "severe cognitive decline". The GDS has been validated against behavioral, neuro-anatomic and neurophysiologic measures [40]. PDU was derived from the nursing homes pharmacists' electronic files and was classified according to the Anatomical Therapeutic Chemical (ATC) classification system into antipsychotics, anxiolytics, hypnotics, antidepressants, anti-epileptics, anti-dementia drugs, and any psychotropic medication

[41]. Medical and demographic data were extracted from the resident's medical files. Data on the dementia subtype, age, gender, length of stay at the SCU, and date of inclusion were recorded.

Statistical analysis

Analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 22. Demographic variables (age, gender, length of stay at the SCU, dementia subtype) were described by calculating means or proportions. Multilevel modeling (random intercept linear mixed model) was used to determine the relationship between the total Qualidem (QoL) score as the dependent variable and age, gender, dementia severity (GDS: mild, moderate, severe), dementia subtype (Alzheimer's dementia, vascular/mixed, frontotemporal dementia, other consisting of lewy body dementia, Parkinson dementia, alcohol related dementia, neurosyphilis and dementia not otherwise specified), the five separate NPI-NH factor scores (summed FxS symptom scores) and PDU (using dichotomous categories: present or absent) as the independent variables. The multilevel model corrected for the clustering of residents in the 13 different SCUs. The explained variance at the resident level was calculated [42]. To investigate the effects of dementia subtype on the relationships between QoL total score and the determinants age, gender, dementia severity (GDS: mild, moderate, severe), five NPI-NH factor scores (summed FxS symptom scores), and PDU (present or absent), the interaction terms of dementia subtype with these determinants were added to the model.

Furthermore, the estimated marginal means of the Qualidem subscale scores were calculated for the dementia subtypes: Alzheimer's, vascular/mixed, and frontotemporal. To compare the estimated means, additional multilevel models were used with the Qualidem subscale scores as the dependent variables and dementia severity, age, and gender as the independent variables. In all analyses, a 2-tailed P value less than .05 was considered statistically significant.

Results

Resident characteristics

A total of 207 residents were included. Mean age was 64 years (SD = 6.1), and the male to female ratio was approximately equal (Table 1). The majority (61.4%) had severe dementia, and most residents were diagnosed with Alzheimer´s dementia (AD) (46.4%). The residents had a mean QoL total score of 76.6 (SD = 16.0) and a mean NPS total score of 24.1 (SD = 19.7). Approximately 68% used at least one psychotropic drug.

Table 1. Demographic and clinical characteristics, Qualidem score, NPI-NH score and PDU (n=207)

Resident age at inclusion	Mean (SD) [Range]	63.9 (6.1) [39-78]
Resident gender	Male n (%)	106 (51.2)
Dementia severity (GDS)	n (%)	
Mild (3,4)		35 (16.9)
Moderate (5)		45 (21.7)
Severe (6,7)		127 (61.4)
Dementia subtype	n (%)	
Alzheimer's dementia		96 (46.4)
Vascular dementia		19 (9.2)
Frontotemporal dementia		62 (30.0)
Lewy body dementia		1 (.5)
Parkinson dementia		1 (.5)
Mixed dementia (AD/VaD)		9 (4.3)
Alcohol related dementia		3 (1.4)
Not otherwise specified (NOS)		8 (3.9)
Other cause		8 (3.9)
Quality of life (Qualidem) [a]	Mean (SD) [Range]	
Care relationship		14.83 (4.6) [4 – 21]
Positive affect		13.23 (4.6) [0 – 18]
Negative affect		6.49 (2.7) [0 – 9]
Restless tense behavior		5.00 (3.0) [0 – 9]
Positive self image		8.19 (1.7) [0 – 9]
Social relations		9.51 (4.4) [0 – 18]
Social isolation		6.69 (2.2) [0 – 9]
Feeling at home		10.15 (2.5) [2 -12]
Something to do		2.50 (2.2) [0 – 6]

Table 1 (no. 24) continued

Total score		76.57 (16.0) [30 – 111]
Neuropsychiatric symptoms (NPI-NH)	FxS score mean (SD) [Range]	
Factor agitation		10.09 (9.8) [0 -48]
Factor depression		2.73 (4.9) [0 – 24]
Factor psychosis		2.20 (4.2) [0 – 21]
Factor psychomotor agitation		4.82 (6.2) [0 – 24]
Factor apathy		5.14 (6.1) [0 – 24]
Total score		24.09 (19.7) [0 - 104]
PDU type of medication (ATC code)	n (%)	
Antipsychotic drugs (N05A)		67 (32.4)
Antidepressant drugs (N06A)		73 (35.3)
Anxiolytic drugs (N05B)		57 (27.5)
Hypnotic/sedatives (N05C)		33 (15.9)
Antiepileptic drugs (N03A)		20 (9.7)
Anti-dementia drugs (N06D)		9 (4.3)
At least one PDU		141 (68.1)

[a]Higher (sub)scores indicate higher QoL

SD: standard deviation; AD = Alzheimer's dementia, VaD = Vascular dementia;

PDU = Psychotropic drug use; GDS = Global Deterioration Scale;

NPI-NH = Neuropsychiatric Inventory-nursing home version;

ATC code = Anatomical Therapeutical Chemical (ATC) classification

Determinants of quality of life

A multilevel model showed that a low QoL was associated with advanced dementia, PDU, and the neuropsychiatric factors agitation/aggression, depression and apathy (Table 2). These variables together accounted for 44% of the variance in total QoL score on the resident level.

Furthermore, after adding the interaction terms to the model, a significant interaction effect between dementia subtype and the factor psychomotor agitation

(p = .046) was found. The relationship between the factor psychomotor agitation and QoL differed between the AD and the FTD groups. Residents with AD who showed high scores on the psychomotor agitation factor experienced a higher QoL (B = .240), whereas residents with FTD showing high scores on the psychomotor agitation factor experienced a lower QoL (B = -.678). No other significant interaction effects were found.

Table 2. Multilevel model with significant correlates of QoL

				95% CI	
	B	Se B	P	Lower bound	Upper bound
Gender (ref. female)	-2.27	1.883	.229	-5.985	1.443
Age	.240	.152	.099	-.059	.539
PDU (ref. none PDU)	-4.863	-1.884	.011*	-8.581	-1.145
Dementia subtype (ref. AD)			.231		
Other	-.780	2.925	.790	-6.550	4.990
Vasc./mixed	-3.280	2.699	.226	-8.600	2.048
FTD	2.699	2.296	.241	-1.830	7.228
AD	0				
Dementia severity (ref. severe)			.005*		
Mild (3,4)	7.410	2.539	.004	2.400	12.420
Moderate (5)	5.070	2.255	.026	.618	9.515
Severe (6,7)	0				
NPI factor agitation	-.528	.111	.000**	-.745	-.312
NPI factor depression	-.670	.204	.001**	-1.071	-.265
NPI factor psychosis	-.181	.242	.455	-.659	.296
NPI factor psychomotor agitation	.042	.159	.793	-.272	.356
NPI factor apathy	-.711	.149	.000**	-1.006	-.416

* < .05 **<.01

Level-one explained proportion of variance = .430

QoL = Quality of life, Qualidem total score; PDU = Psychotropic drug use;

AD= Alzheimer's dementia; Vasc./mixed = Vascular/ mixed dementia;

FTD = Frontotemporal dementia; NPI-NH = Neuropsychiatric Inventory

Difference in quality of life domains between dementia subtypes

The multilevel models showed that residents with FTD scored higher on the 'Care relationship' subscale than residents with vasc./mixed dementia (mean 16.02 versus 13.26, p = .012) (Table 3). The scores on the subscale 'Negative affect' were lower in residents with AD compared to residents with FTD (mean 5.75 versus 7.02, p = .007). Residents with FTD scored higher on the subscale 'Positive self-image' compared to residents with vasc./mixed dementia (mean 8.49 versus 7.45, p = .012). Additionally, the score on the subscale ´Feeling at home´ was higher in residents with FTD than in residents with vasc./mixed dementia (mean 10.04 versus 8.67, p = .014). Finally, residents with FTD scored lower on the subscale 'Social relations' than residents with AD (mean 9.77 versus 11.71, p = .005) and with vasc./mixed dementia (mean 9.77 versus 12.16, p = .007).

Table 3. Differences QoL between Alzheimer's dementia, Vascular/mixed and Frontotemporal dementia groups

	AD (n= 96)	Vasc./ mixed (n=28)	FTD (n= 62)	P
Qualidem subscale scores [a]				
Estimated mean				
Care relationship	14.41	13.26	16.02	.030*
Positive affect	14.53	13.71	12.97	.162
Negative affect	5.75	6.50	7.02	.023*
Restless tense behavior	5.23	5.61	5.82	.505
Positive self image	7.87	7.45	8.49	.029*
Social relations	11.71	12.16	9.77	.006**
Social isolation	6.91	6.57	6.90	.771
Feeling at home	9.78	8.67	10.04	.039*
Something to do	3.12	3.78	2.97	.140

* < .05 **<.01

[a]Higher subscale scores indicate higher QoL

QoL = Quality of life; AD= Alzheimer's dementia; Vasc./mixed = Vascular/ mixed dementia; FTD = Frontotemporal dementiaAll outcome variables are adjusted for age, gender, and dementia severity.

Discussion

In this study we found that the residents' QoL was negatively associated with advanced dementia, PDU, and the factors agitation/aggression, depression, and apathy. The model showed that all the variables included accounted for 44% of the variance in the total QoL score. The relationship between QoL and the determinants studied did not differ for dementia subtypes, with the exception of the factor psychomotor agitation. Although no association was found between overall QoL and dementia subtype, we did find differences between residents with AD, vasc./mixed dementia and FTD regarding the separate QoL domains.

Our findings suggest that the same determinants of QoL in LOD also apply to YOD nursing home residents. Advanced dementia was found associated with poor QoL in nursing home residents with LOD [12]. Also, similar to our findings, PDU, agitation and depression have been found negatively associated with QoL in LOD [7]. Furthermore, in LOD, a relationship between poorer QoL and high levels of apathy was found [8]. Therefore, this might suggest that the high rates of NPS and PDU found in residents with YOD indeed place younger residents with dementia in particular at risk of experiencing poor QoL [24,25].

Furthermore, residents with FTD scored better on four QoL domains. This might appear counterintuitive because of the higher levels of agitation, apathy, disinhibition and irritability found in FTD [43,44]. An explanation for this finding could be that FTD is characterized by an early loss of disease awareness, which has been found to be associated with the occurrence of fewer depressive symptoms and might also have a positive influence on self-image [45,46]. Our findings are also consistent with a recent study on community-dwelling people with YOD, which indicated that people with FTD rated their own QoL higher than other subtypes of dementia [26]. Therefore, people with FTD might communicate less problems and negative emotions towards health care professionals influencing reliability of proxy-reports of their QoL. Furthermore, institutionalization provides a structured environment, which might have a particular advantage for people with FTD because of the higher levels of apathy found in FTD (41). We also found that residents with FTD appeared to experience a lower quality of social relationships. This finding could be explained by the higher levels of agitation, apathy, disinhibition and irritability found in residents with FTD [43,44], as these characteristics might invoke negative reactions from other residents, hinder social interactions and therefore result in poorer quality of social relationships.

Several limitations of this study should be considered. We used the total score on the Qualidem to reduce the number of tests and therefore diminish the risk of a Type

1 error. The use of the Qualidem total score also enabled a comparison of our results with those of other studies on the determinants of QoL in LOD using a similar methodology. However, we should be aware that using this total score might have resulted in a loss of information by not taking into account the multidimensionality of the construct of QoL. Another inevitable limitation of this study was the use of proxy reports to investigate residents' QoL. Dröes et al. (2006) found that there were differences in the perspectives on QoL between people with dementia and their caregivers [29]. Also, the younger age of our residents could have influenced the proxy reports. Nurses might be more inclined to observe a lower QoL in YOD, because dementia is considered a disease of old age. Having this disease at a younger age might be considered to have a more negative influence on wellbeing. However, most residents in this study had advanced dementia. Even when sufficient communicative abilities were present, their severe cognitive impairments likely would have threatened the validity of self-reported results. Nonetheless, we should be aware that the QoL ratings could have been influenced by the professional caregivers' attitudes towards the resident and dementia [10,12,16]. Furthermore, we should be aware that correlations between the Qualidem subscales and NPI factors could have influenced the explained variance to some degree. Also, other factors possibly contributing to the QoL of residents with YOD (e.g. nursing home environment, physical impairments, pain, frequency of visits from family members) have not been studied. Additionally, the residents in this study were only recruited from nursing homes which were affiliated with the Dutch YOD Knowledge Center. Therefore selection bias might have taken place possibly influencing the external validity of our findings. Finally, some caution should be used when interpreting the findings of the subgroup analyses investigating the interaction effects and the multilevel models with Qualidem subscale scores as the dependent variables. Considering the large number of tests in the analyses, there was a risk of Type 1 error in these subgroup analyses this might have been reflected in the differences observed in the effects of psychomotor agitation on QoL between dementia subtypes, as there is no apparent explanation for this finding. Also, vascular dementia and mixed dementia were combined in order to gain statistical power. However, as those dementia subtypes might differ in phenomenology, this could have partly influenced the results. Further testing in future studies including larger groups of less common diagnoses is necessary to confirm the differences in the determinants of QoL and QoL profiles between dementia subtypes found in our exploratory analyses.

This study provides important insight into the determinants of QoL in nursing home residents with YOD. The high rates of NPS and PDU in nursing home residents with

YOD [24] raise concern given the strong associations found in this study between these variables and QoL. Furthermore, our results challenge the existing pharmacological interventions in the treatment of NPS, as PDU by itself also is negatively associated with QoL in YOD. This finding is in line with other studies on QoL in LOD [7,5,18]. Therefore, in the treatment of NPS, the wellbeing of nursing home residents with YOD will probably benefit most from non-pharmacological interventions specifically aimed at reducing agitation/aggression, depression, and apathy. More research is needed on the influence of PDU on QoL in YOD taking into account the specific categories of psychotropic medication as well as duration, usage, dose, and causality.

Additionally, our results suggest that nursing home residents with AD and vasc./mixed dementia might benefit more from interventions to prevent or diminish the risk of experiencing negative emotions (e.g. supporting conversations with a health care professional, regular check for depressive symptoms, avoid confrontation with their inabilities). On the other hand, in order to improve their quality of social relationships, nursing home residents with FTD might benefit from interventions aimed at increasing positive social interaction for instance with family, other nursing home residents or volunteers. Health care professionals should receive education to raise their awareness about the possible differences between dementia subtypes regarding aspects of QoL and therewith ensure that they will provide care that meets the specific care needs of all diagnostic groups in order to improve residents' QoL.

References

1. Ettema TP, Droes RM, de Lange J, Mellenberg GJ, Ribbe MW: A review of quality of life instruments used in dementia. Quality of life research 2005;14:675-686.
2. Hurt CS, Banerjee S, Tunnard C, et al.: Insight, cognition and quality of life in alzheimer's disease. J Neurol Neurosurg Psychiatry 2010;81:331-336.
3. Thomas P, Lalloue F, Preux PM, et al.: Dementia patients caregivers quality of life: The pixel study. Int J Geriatr Psychiatry 2006;21:50-56.
4. Bostrom F, Jonsson L, Minthon L, Londos E: Patients with dementia with lewy bodies have more impaired quality of life than patients with alzheimer disease. Alzheimer Dis Assoc Disord 2007;21:150–154.
5. Gonzalez-Salvador T, Lyketsos CG, Baker A, et al.: Quality of life in dementiapatients in long-term care. Int J Geriatr Psychiatry 2000;15:181-189.
6. Sloane PD, Zimmerman S, Williams CS, et al.: Evaluating the quality of life of long term care residents with dementia. Gerontologist 2005;45:37–49.
7. Wetzels R, Zuidema S, de Jonghe J, Verhey F, Koopmans R: Determinants of quality of life in nursing home residents with dementia. Dementia and Geriatric Cognitive Disorders 2010;29:189-197.
8. Samus QM, Rosenblatt A, Steele C, et al.: The association of neuropsychiatric symptoms and environment with quality of life in assisted living residents with dementia. Gerontologist 2005;45:19–26.
9. Banerjee S, Smith SC, Lamping DL, et al.: Quality of life in dementia: More than just cognition: An analysis of associations with quality of life in dementia. J Neurol Neurosurg Psychiatry 2006;77:146–148.
10. Hoe J, Hancock G, Livingston G, Orrell M: Quality of life of people with dementia in residential care homes. Br J Psychiatry 2006;188:460–464.
11. Ettema TP, Droes RM, de Lange J, Mellenberg GJ, Ribbe MW: Qualidem: Development and evaluation of a dementia specific quality of life instrument-validation. Int J Geriatr Psychiatry 2007;22:424-430.
12. Winzelberg GS, Williams CS, Preisser JS, Zimmerman S, Sloana PD: Factors associated with nursing assistant quality-of-life ratings for residents with dementia in long-term care facilities. Gerontologist 2005;45:106–114.
13. Hurt C, Bhattacharyya S, Burns A, et al.: Patient and caregiver perspectives of quality of life in dementia. An investigation of the relationship to behavioural and psychological symptoms in dementia. Dementia and Geriatric Cognitive Disorders 2008;26:138-146.

14. Logsdon RG, Gibbins LE, McCurry SM, Teri L: Assessing quality of life in older adults with cognitive impairments. Psychosom Med 2002;64:510–519.

15. Bruvik FK, Ulstein ID, Ranhoff AH, Engedal K: The quality of life of people with dementia and their family carers. Dementia and Geriatric Cognitive Disorders 2012;34:7-14.

16. Nakanishi K, Hanihara T, Mutai H, Nakaaki S: Evaluating the quality of life of people with dementia in residential care facilities. Dementia and Geriatric Cognitive Disorders 2011;32:39-44.

17. Yeager CA, Hyer L: Apathy in dementia: Relations with depression, functional competence, and quality of life. Psychol Rep 2008;102:718–722.

18. Ballard CG, Margallo-Lana ML: The relationship between antipsychotic treatment and quality of life for patients with dementia living in residential and nursing home care facilities. J Clin Psychiatry 2004;65:23-28.

19. van Vliet D, de Vugt ME, Bakker C, et al.: Time to diagnosis in young-onset dementia as compared with late-onset dementia. Psychological Medicine 2012;42:423-432.

20. van Vliet D, de Vugt ME, Bakker C, Koopmans RTCM, Verhey FRJ: Impact of early onset dementia on caregivers: A review. International Journal of Geriatr Psychiatry 2010;25:1091–1100.

21. Harris PB, Keady J: Selfhood in younger onset dementia: Transitions and testimonies. Aging & Mental Health 2009;13:437-444.

22. Harris PB, Keady J: Living with early onset dementia: Exploring the experience and developing evidence-based guidelines for practice. Alzheimer's Care Quarterly 2004;5:111-122.

23. van Vliet D, de Vugt ME, Aalten P, et al.: Prevalence of neuropsychiatric symptoms in young-onset compared to late-onset alzheimer's disease - part 1: Findings of the two year longitudinal needyd-study. Dementia and Geriatric Cognitive Disorders 2012;34:319-327.

24. Mulders AJMJ, Fick IWF, Bor H, et al.:Prevalence and correlates of neuropsychiatric symptoms in nursing home patients with young-onset dementia: The beyond study. JAMDA 2016;17:495-500.

25. Mulders AJMJ, Zuidema SU, Verhey FR, Koopmans RTCM: Characteristics of institutionalized young onset dementia patients – the beyond study. International Psychogeriatrics 2014;12:1973–1981.

26. Bakker C, de Vugt ME, van Vliet D, et al.: Unmet needs and health-related quality of life in young onset dementia. The American Journal of Geriatric Psychiatry 2014;22:1121-1130.

27. Baptista MAT, Santos RL, Kimura N, et al.: Quality of life in young onset dementia: An updated systematic review. Trends in psychiatry and psychotherapy 2016;38:6-13.
28. Ettema TP, Droes RM, de Lange J, Mellenbergh GJ, Ribbe MW: Qualidem: Development and evaluation of a dementia specific quality of life instrument. Scalability, reliability and internal structure. Int J Geriatr Psychiatry 2007;22:549-556.
29. Droes RM, Boelens- van der Knoop ECC, Bos J, Meihuizen L, et al.: Quality of life in dementia in perspective. Dementia Sage publications 2006;5:533-558.
30. Klapwijk MS, Caljouw MMA, Pieper MJC, van der Steen JT, Achterber WP: Characteristics associated with quality of life in long-term care residents with dementia: A cross-sectional study. Dementia and Geriatric Cognitive Disorders 2016;42:186-197.
31. American Psychiatric Association: Diagnostic and statistical manual of mental disorders- text revision: DSM-IV-TR. Washington DC, American Psychiatric Association, 2000, vol 1, pp 943.
32. Gorno-Tempini ML, Hillis AE, Weintraub S, et al.:Classification of primary progressive aphasia and its variants. Neurology 2011;76:1006-1014.
33. McKeith IG: Consensus guidelines for the clinical and pathologic diagnosis of dementia with lewy bodies (dlb): Report of the consortium on dlb international workshop. Journal of Alzheimer's Disease 2006;9:417-423.
34. McKhann G, Drachman D, Folstein M, et al.: Clinical diagnosis of alzheimer's disease: Report of the nincds-adrda work group under the auspices of department of health and human services task force on alzheimer's disease. Neurology 1984;34:939 944.
35. Rascovsky K, Hodges JR, Knopman D, et al.: Sensitivity of revised diagnostic criteria for the behavioural variant of frontotemporal dementia. Brain : a journal of neurology 2011;134:2456-2477.
36. Roman GC, Tatemichi TK, Erkinjuntti T, et al.: Vascular dementia: Diagnostic criteria for research studies. Report of the ninds-airen international workshop. Neurology 1993;43:250-260.
37. Kat MG, de Jonghe JF, Aalten P, et al.: Neuropsychiatric symptoms of dementia: Psychometric aspects of the dutch neuropsychiatric inventory (npi). Tijdschrift voor Gerontologie en Geriatrie 2002;33:150-155.
38. Kaufer DI, Cummings JL, Ketchel P, et al.: Validation of the npi-q, a brief clinical form of the neuropsychiatric inventory. The Journal of neuropsychiatry and clinical neurosciences 2000;12:233-239.

39. Zuidema SU, de Jonghe JFM, Verhey FRJ, Koopmans RTCM: Neuropsychiatric symptoms in nursing home patients: Factor structure invariance of the dutch nursing home version of the neuropsychiatric inventory in different stages of dementia. Dement Geriatr Cogn Disord 2007;24:169–176.

40. Reisberg B, Ferris SH, de Leon MJ, Crook T: The global deterioration scale for assessment of primary degenerative dementia. The American Journal of Psychiatry 1982;139:1136–1139.

41. WHO: Anatomical therapeutical chemical (atc) classification index including defined daily doses (ddds) for plain substances. Oslo, World Health Organisation Collaborating Centre for Drug Statistics Methodology, 1997.

42. Snijders TAB, Bosker RJ: Multilevel analysis: An introduction to basic and advanced multilevel modeling. London, Sage Publishers, 2012.

43. De Vugt ME, Riedijk SR, Aalten P, et al.: Impact of behavioural problems on spousal caregivers: A comparion between alzheimer's disease and frontotemporal dementia. Dement Geriatr Cogn Disord 2006;22:35-41.

44. Shuling Liu, Yi Jin, Zhihong Shi, et al.: The effects of behavioral and psychological symptoms on caregiver burden in frontotemporal dementia, lewy body dementia, and alzheimer's disease: Clinical experience in china. Aging and Mental Health 2016;21(6):651-657.

45. van Vliet D, de Vugt ME, Kohler S, et al.: Awareness and its association with affective symptoms in young-onset and late-onset alzheimer disease: A prospective study. Alzheimer Dis Assoc Disord 2013;27:265-271.

46. Perry RJ, Miller BL: Behavior and treatment in frontotemporal dementia. Neurology 2001;56:S46–S51.


Family
I'm glad I
I love you
I wish I could remember
Pain
New challe
help
happiness
love
love life
how
Take care of the children
I forgot
I don't know
Golden years
enjoy
Good life
Work
learning
why
angry
I have
Friends
to grow
away from home
the beginning

Chapter 3

NEUROPSYCHIATRIC SYMPTOMS IN NURSING HOME RESIDENTS WITH YOUNG-ONSET DEMENTIA

Differences in neuropsychiatric symptoms between nursing home residents with young-onset dementia and late-onset dementia

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Abstract

Objective: The aims of the current study are (1) to explore the differences in neuropsychiatric symptoms (NPS) between two large samples of nursing home (NH) residents with young-onset dementia (YOD) and late-onset dementia (LOD), and (2) to investigate whether the possible differences can be attributed to differences in dementia subtype (Alzheimer's dementia, vascular dementia, or other), gender, psychotropic drug use (PDU), or dementia severity.

Method: This is a retrospective cross-sectional study in Dutch long-term care facilities. 386 NH residents with YOD and 350 with LOD were included. Multilevel modeling was used to compare NPS between the groups (YOD versus LOD). Furthermore, dementia subtype, gender, PDU, and dementia severity were added to the crude multilevel models to investigate whether the possible differences in NPS could be attributed to these characteristics.

Results: Higher levels of apathy were found in NH residents with YOD. After dementia subtype, gender, PDU, and dementia severity were added to the models, also lower levels of verbally agitated behaviors were found in YOD compared to LOD.

Conclusion: Considering the higher levels of apathy found in NH residents with YOD, we recommend that special attention be paid to interventions targeting apathy in YOD. Although no differences in other NPS were found, the PDU rates were higher in YOD, suggesting that the threshold for the use of PDU in the management of NPS is lower. This underscores the need for appropriate attention to non-pharmacological interventions for the management of NPS in YOD.

Introduction

Young-onset dementia (YOD) is defined as dementia with symptom onset before the age of 65. In YOD, neuropsychiatric symptoms (NPS), such as apathy, agitation, aggression, and hallucinations, are highly prevalent [1,2]. A recent Dutch study showed that 90% of nursing home (NH) residents with YOD had one or more NPS [2]. Previous research in late-onset dementia (LOD) has shown that NPS often result in negative health outcomes such as a loss of quality of life (QoL), increased cost of care, and high workload for the NH staff [3-5].

People with YOD may have a higher risk of developing NPS compared to people with LOD. For example, in the YOD NH population more than half of the residents are male, compared to 20% of the residents in the LOD NH population [1,6]. Extreme NPS seem especially likely to occur in men below the age of 70 years, as these residents are stronger and more vital [7]. Additionally, people with YOD are cared for at home for a longer period than people with LOD [8]. Therefore, dementia might be more advanced in NH residents with YOD compared to LOD at the time of institutionalization. Increased severity of dementia has been linked to more NPS (such as agitation, aggression, and apathy) in NH residents with YOD and LOD [2, 9]. In addition, frontotemporal dementia (FTD) is more common in YOD; higher levels of agitation, disinhibition, and irritability are found in people with FTD than in those with AD, at least in the community-dwelling population [1, 10-12].

To develop effective treatment and further enhance care for NH residents with YOD, it is important to gain more insight into the differences in NPS between NH residents with YOD and LOD and the specific characteristics of YOD that might give rise to these possible differences. This insight supports health-care professionals to direct treatment and provide care that meets the specific care needs of younger NH residents.

There have been a few studies that directly compared rates of NPS between YOD and LOD. However, these studies did not take into account the possible influence of psychotropic drugs, which are often used in the treatment of NPS. Higher rates of psychotropic drug use (PDU) are found in NH residents with YOD (87%) than in those with LOD (ranging from 63%-75%) [2, 13-15]. Therefore, a greater decline in NPS due to treatment with PDU might be expected in YOD. Furthermore, to our knowledge, all these studies involve people with Alzheimer's dementia (AD), while NPS in other common types of dementia in YOD, such as FTD, were not taken into account.

In NPS studies directly comparing young-onset AD (YO-AD) and late-onset AD (LO-AD), the results suggest less NPS overall in people with YO-AD than in those with LO-AD, at least in a community-dwelling population. For instance, Toyota et al. (2007) compared

NPS between community-dwelling people with YO-AD and LO-AD and did not find differences regarding the prevalence of depressive symptoms and anxiety [16]. Moreover, they found fewer delusions and hallucinations as well as less agitation, disinhibition, and aberrant motor behavior in YO-AD than in LO-AD. Van Vliet et al. (2012) also found lower incidence and prevalence rates of NPS in community-dwelling people with YO-AD than in those with LO-AD [17]. In addition, Mushtaq et al. (2016) found higher levels of delusions, agitation, anxiety, disinhibition and nighttime behavioral disturbances in community-dwelling people with LO-AD than in those with YO-AD [18]. In contrast, the only study to our knowledge comparing NPS in YOD and in LOD NH residents found higher levels of behavioral symptoms (e.g., waking up at night, aimless wandering, hiding things) in NH residents with YO-AD than in residents with LO-AD among people >90 years old [19].

The aims of the current study are (1) to explore the differences in NPS between two large samples of NH residents with YOD and LOD, and (2) to investigate whether possible differences can be attributed to differences in dementia subtype (Alzheimer's dementia, vascular dementia, or other subtypes including FTD), gender, psychotropic drug use (PDU), or dementia severity.

Methods

Subjects

This retrospective cross-sectional study is part of the Behavior and Evolution of Young-ONset Dementia part 2 (Beyond-II) study, a multicenter intervention study aimed at improving the management of NPS in institutionalized people with YOD (N = 203 YOD NH residents) [20]. Additional baseline data were used from two other longitudinal studies: the Beyond-I study (N = 185 YOD NH residents) and the 'Grip on challenging behavior study' (N = 362 LOD NH residents) [1, 21]. These studies used the same assessment instruments as the Beyond-II study.

In the Netherlands, a large proportion of nursing homes have YOD special care units (YOD-SCUs) delivering specialized care for people with YOD. In the YOD group, only YOD-SCUs participated. Residents in the YOD group were included in this study if they had a dementia diagnosis with symptom onset before the age of 65 and had been residing in the YOD-SCU for at least one month before inclusion. The dementia diagnosis was established before inclusion in the study according to the 4th edition of the Diagnostic and Statistical Manual of Mental Disorders, Text Revision (2000) [22]. In the YOD group, internationally accepted criteria for diagnosing dementia subtypes were used [23-27]. The diagnosis was

retrieved from the medical file. The exclusion criteria were lack of informed consent, dementia caused by human immunodeficiency virus (HIV), traumatic brain injury, Down's syndrome, Korsakoff syndrome, Huntington's disease, or alcohol-related dementia. In the Beyond-II study, informed consent was obtained from the residents' legal representative and the informed consent rate was 88%. In the Beyond-I study, the residents or their legal representatives had the possibility to object to participation, resulting in a participation rate of 99%. Some YOD-SCUs participated in both the Beyond-I and Beyond-II studies. When residents had the same gender, date of birth, and diagnosis, one of them was randomly excluded from either the Beyond-I or Beyond-II sample used in this study to prevent duplicates.

In the LOD group, participating units for people with dementia (dementia special care units, DSCUs) were recruited from NHs that collaborate with the VU University Medical Center (Amsterdam) and the Radboud University Medical Center Nijmegen [21]. The same inclusion criteria (other than symptom onset before the age of 65) as in the YOD sample were applied in this study to obtain homogenous samples. Additionally, residents in the LOD group with an age of 70 years or younger were excluded to diminish the risk of YOD residents being part of the LOD group. Residents in the YOD group with an age of 70 years of older were not excluded, because they all had a symptom onset before the age of 65; therefore, there was no risk that they were part of the LOD group. In the LOD group, legal representatives of the residents had the possibility to object to participation, resulting in a participation rate of 99%.

Data collection and assessments

The Beyond-I and Beyond-II study protocols were approved by the Medical Ethics Committee region Arnhem/Nijmegen. The Grip on challenging behavior study protocol was approved by the Medical Ethics Review Committee of the VU University Medical Center. This research project was performed according to the principles of the Declaration of Helsinki (version November 2013, www.wma.net) and is in agreement with the law regarding medical-scientific research in humans (WMO). Trained researchers and research assistants collected the data through structured interviews with the nursing staff and from the resident's medical files. Respondents were considered reliable if they were the vocational nurse specifically assigned to the resident or had regular contact with the resident in the past month.

Outcome measures

Neuropsychiatric symptoms (NPS) were assessed with the Dutch version of the Neuropsychiatric Inventory-Nursing Home Version (NPI-NH). The NPI-NH has high interrater reliability and has been found to be a valid instrument for the assessment of a wide range of NPS in dementia [28-29]. The NPI-NH consists of ten NPS (delusions, hallucinations, agitation/aggression, depression, anxiety, euphoria/elation, apathy/indifference, disinhibition, irritability/lability, aberrant motor behavior) and two neurovegetative symptoms (nighttime behavior disturbances and appetite/eating disturbances). For each symptom, a screening question is used to determine whether the symptom is present. If the symptom is present, Frequency (F) and Severity (S) are rated on a four-point (ranging from 1-4) and three-point Likert-scale (ranging from 1-3), respectively, for each symptom. Scores for each symptom are calculated as F x S. We were interested in all NPS, including symptoms with a low frequency or severity and also when symptoms were not present. Therefore, we also included symptoms with a low frequency and severity in our analyses (instead of focusing on only clinical relevant behavior F x S ≥ 4) and chose to score F x S as 0 when a symptom was not present. A total score is calculated by summing the F x S scores (ranging from 0 to 144). Five NPI-NH factor scores were calculated by summing the symptom scores (F x S) included in each factor: (1) agitation/aggression, consisting of the agitation/aggression, euphoria, disinhibition and irritability symptom scores; (2) depression, consisting of the depression and anxiety symptom scores; (3) psychosis, consisting of the delusion and hallucination symptom scores; (4) psychomotor agitation, consisting of the aberrant motor behavior and nighttime behavior symptom scores; and (5) apathy, consisting of the apathy and eating disorder symptom scores. These neuropsychiatric factors have been found to be relatively consistent in nursing home residents with dementia, across different stages of dementia [30].

The Dutch version of the Cohen-Mansfield Agitation Inventory (CMAI-D) was used to assess *agitation and aggression* [31, 31]. The CMAI has well-established validity and reliability and assesses 29 agitated or aggressive behaviors [32]. The frequency of each symptom is rated on a seven-point scale (range 1-7) ranging from never to several times an hour. The total CMAI score ranges from 29 to 203. We used CMAI factors based on a previous study in which three CMAI factors in a large NH sample were found: physically non-aggressive behaviors (range 7-49), physically aggressive behaviors (range 8-56), and verbally agitated behaviors (range 4-28) [33].

Other measures

Dementia severity was assessed with the Global Deterioration Scale (GDS) [34]. The GDS describes seven different stages of dementia on a seven-point scale (1-7), ranging from "subjectively and objectively normal cognition" to "severe cognitive decline". The GDS has been validated against behavioral, neuro-anatomical and neurophysiological measures, for which significant correlations were found [34].

In addition, data on *dementia subtype, age, gender and length of stay* at the YOD-SCU or DSCU were collected from resident's medical files. Psychotropic drug use (PDU) was derived from the nursing homes pharmacists' electronic files and was classified according to the Anatomical Therapeutic Chemical (ATC) classification system (1997) into antipsychotics, anxiolytics, hypnotics, antidepressants, anti-epileptics, anti-dementia drugs, and any psychotropic medication [35].

Statistical analysis

All analyses were performed using Statistical Package for the Social Sciences (SPSS) version 22. Before analysis, the data were checked for missing values. If the proportion of missing values in the CMAI total and factor scores was 20% or less, the missing items were replaced with the mean of the remaining items. It was not possible to use mean imputation on the NPI-NH factor scores, GDS, or PDU, as these scores consisted of less than 5 items, and even a single missing value would constitute more than 20% of the items. Therefore, residents with missing items on the NPI-NH symptom scores, GDS, and PDU were excluded from analysis.

Demographic variables for both groups (LOD and YOD) were described by calculating means or proportions. Multilevel modeling (random intercept linear mixed models) was used to compare the mean CMAI total, CMAI factor (physically aggressive behaviors, physically nonaggressive behaviors, verbally agitated behaviors), NPI-NH total, and NPI-NH factor (agitation, depression, psychosis, psychomotor agitation, apathy) scores as dependent variables, with group (YOD versus LOD) as an independent variable. Multilevel modeling allows correction for the clustering of residents in different health care organizations and therefore also for possible differences in cohorts as each health care organization was part of a specific cohort. Furthermore, to investigate whether the possible differences could be attributed to differences in dementia subtype (AD, vascular dementia, or other subtypes including FTD), gender, psychotropic drug use (using dichotomous categories: present or absent), or dementia severity (GDS: mild, moderate, severe), we added these variables to the crude multilevel models.

Results

Resident characteristics

A total of 736 residents were included, of whom 386 residents had YOD and 350 had LOD. In the YOD group, the ratio of males to females was approximately equal (49.5% female), in contrast to the LOD group, in which a large majority of subjects were female (73.7%). In both the YOD and LOD group, most residents had Alzheimer's dementia (43.3% in YOD and 48.6% in LOD). The second most prevalent dementia subtype was vascular dementia (35.1%) in the LOD group and frontotemporal dementia (FTD) (25.1%) in the YOD group. In both YOD and LOD, most residents had advanced dementia (62.7% in YOD and 76.8% in LOD). Furthermore, psychotropic drug use (PDU) seemed more common in the YOD group (76.9% in YOD versus 55.1% in LOD) (Table 1).

Table 1. Demographic and clinical characteristics of the YOD and LOD group

		YOD N = 386	LOD N = 350
Resident age at inclusion	Mean (SD) [Range]	62.4 (6.9) [39-78]	84.43 (6.3) [71-102]
Resident gender	Male n (%)	195 (50.5)	92 (26.3)
Dementia severity (GDS)[a]	n (%)		
Mild (2,3,4)		62 (16.1)	13 (3.7)
Moderate (5)		81 (21.0)	66 (18.9)
Severe (6,7)		242 (62.7)	267 (76.3)
Dementia subtype	n (%)		
Alzheimer's disease		167 (43.3)	170 (48.6)
Vascular dementia		56 (14.5)	123 (35.1)
Frontotemporal dementia		97 (25.1)	7 (2.0)
Other		66 (17.1)	50 (14.3)
PDU (at least one) [b]	n (%)	297 (76.9)	193 (55.1)
CMAI total score	Mean (SD)	49.60 (18.37)	50.55 (18.21)
CMAI factor scores [c]	Mean (SD)		
Physically aggressive behaviors		13.55 (6.51)	13.88 (6.36)
Physically nonaggressive behaviors		14.38 (7.97)	13.87 (7.72)
Verbally agitated behaviors		8.37 (5.99)	9.24 (5.96)

Table 1 (no. 45) continued

NPI-NH total score	Mean (SD)	22.84 (17.77)	21.22 (17.80)
NPI-NH factor scores	Mean (SD)		
Agitation		9.93 (10.21)	9.96 (9.65)
Depression		3.11 (5.17)	4.12 (5.31)
Psychosis		1.79 (3.92)	2.26 (4.37)
Psychomotor agitation		4.84 (6.22)	3.97 (5.47)
Apathy		5.95 (5.97)	3.46 (4.96)

[a] 1 missing in YOD group, 4 missing in LOD group

[b] 8 missing in LOD group

[c] 1 missing in YOD group, 6 missing in LOD group

SD: standard deviation, GDS = Global Deterioration Scale, PDU = Psychotropic Drug Use, CMAI = Cohen-Mansfield Agitation Inventory, NPI-NH = Neuropsychiatric Inventory-nursing home version.

Differences in NPS between YOD and LOD

The unadjusted multilevel models showed that residents with YOD had higher mean NPI-NH apathy factor scores than residents with LOD ($p < .001$, $B = 2.612$) (Table 2, model 1). No other statistically significant differences were found on either the NPI-NH or the CMAI factor scores. After entry of PDU, gender, dementia severity and dementia subtype into the multilevel models, significant differences in both the apathy score ($p < .001$ $B = 2.794$) and the mean CMAI verbally agitated behaviors factor score were found ($p = .023$, $B = -1.403$) (Table 2, model 2). Residents with YOD had lower mean CMAI verbally agitated behaviors factor scores compared to residents with LOD.

Table 2. Multilevel models with differences between groups (YOD / LOD) on NPS with no correction (Model 1), and correction for gender, PDU, dementia severity, and dementia subtype (Model 2).

	Model 1				Model 2			
			95% CI				95% CI	
	B	P	Lower bound	Upper bound	B	P	Lower bound	Upper bound
CMAI total score	-.316	.900	-5.386	4.753	-1.480	.544	-6.365	3.406
CMAI factor scores								
Physically aggressive behaviors	-.236	.766	-1.833	1.361	-.234	.751	-1.711	1.243
Physically nonaggressive behaviors	.761	.440	-1.22	2.743	.426	.673	-1.510	2.451
Verbally agitated behaviors	-.827	.115	-1.865	.211	-1.403	.023*	-2.600	-.206
NPI-NH total score	2.047	.342	-2.271	6.364	1.597	.444	-2.573	5.766
NPI-NH factor scores								
Agitation/ Aggression	.061	.943	-1.658	1.780	-1.002	.270	-2.478	1.036
Depression	-.972	.117	-2.201	.258	-.710	.221	-1.866	.446
Psychosis	-.419	.387	-1.393	.555	-.490	.341	-1.519	.539
Psychomotor agitation	.988	.143	-.349	2.324	.708	.335	-.761	2.178
Apathy	2.612	.000**	1.251	3.972	2.794	.000**	1.502	4.086

* < .05 **<.01

CMAI = Cohen-Mansfield Agitation Inventory; NPI-NH = Neuropsychiatric Inventory-nursing home version; PDU = Psychotropic drug use

Discussion

In this study, the differences in NPS between heterogeneous samples of NH residents with YOD and LOD were investigated. Higher levels of apathy were found in NH residents with YOD compared to LOD. Furthermore, after corrections were applied for gender, PDU, dementia severity, and dementia subtype, higher levels of verbally agitated behaviors were found in LOD than in YOD.

In line with our findings, Cohen-Mansfield and Libin (2005) found that higher levels of verbal agitation were associated with older age [36]. An explanation could be that with advanced age, more physical impairments are likely to occur, hindering activities in daily life. This likely results in feelings of frustration and as a consequent an increase in verbally agitated behaviors in response to the high levels of physical impairment. Higher rates of verbal aggression in LOD were only found in our study after taking into account the influence of possible confounders (gender, PDU, dementia subtype, dementia severity). An explanation could be the higher prevalence of residents with less advanced dementia in the YOD group, as verbally agitated behavior is less prevalent in advanced dementia [2]. Furthermore, we did not find differences in the CMAI total or other factor scores, which supports the notion that agitation is a multidimensional construct consisting of different aspects that should be taken into account in further research in order to prevent loss of information.

We found higher levels of apathy in NH residents with YOD than in those with LOD. This might be partly explained by the high prevalence in YOD of FTD, in which higher rates of apathy have been found compared to AD [12]. However, these differences were still strongly significant after dementia subtype was corrected for, suggesting that higher rates of apathy exist in NH residents with YOD, irrespectively of dementia subtype. Another explanation might be that the frequency and severity of the NPS (including apathy) were rated by nursing staff members. Nurses might observe apathy in LOD less often because they might perceive the inactivity as part of older age. Although apathy is often not experienced as disturbing by nursing staff, the higher rates found in NH residents with YOD still raise concern because of the strong negative association between apathy and quality of life in NH residents with YOD [37, 5]. Therefore, special attention needs to be directed to interventions targeting apathy in NH residents with YOD.

Although we did not find any additional differences in NPS between the two groups, the PDU rates in YOD seemed higher than those of the LOD group (77% in YOD versus 55% in LOD). This suggests that the threshold for the use of psychotropic drugs in

the management of NPS is lower in YOD. An explanation for the higher levels of PDU in YOD could be that the same behaviors in younger individuals are perceived as more threatening or distressing by the nursing staff. Consequently, physicians might be more inclined to prescribe psychotropic drugs in YOD than in LOD [38]. In future studies, further testing is needed on differences in distress experienced by YOD and LOD nursing staff in response to residents' NPS.

Several limitations of this study should be considered. We chose to use factor scores instead of symptom scores on the NPI-NH in order to reduce the number of tests in the analyses and thereby diminish the risk of a Type 1 error. Additionally, we used factor scores of the CMAI instead of the total score to provide clarity regarding the possible differences in specific aspects of aggression and thereby prevent a loss of information. However, the factor structure of both the NPI-NH and CMAI was evaluated in older NH residents with dementia and has not yet been established in YOD [30, 33]. Furthermore, part of the YOD group was drawn from an older cohort. There is a possibility that there are differences within these cohorts (for example, due to changes in the health care system), for which we partly corrected with the use of the multilevel models. At last, we cannot confirm that the international accepted criteria for diagnosing dementia subtypes were used in all residents part of the LOD group.

Conclusion

This study provides important insight into the differences in NPS between NH residents with YOD and LOD. The higher rates of apathy found in NH residents with YOD raise concern because of the strong negative association between apathy and quality of life [37]. Therefore, in order to improve care, we recommend that special attention be paid to interventions targeting apathy in NH residents with YOD. For example, especially for NH residents with YOD, it might be important to provide a stimulating socio-therapeutic environment and to facilitate social engagement and activities of daily living. Further research is needed to gain insight into possible biological or psychosocial influences underlying the differences in apathy between NH residents with YOD and LOD.

Although NH residents with YOD were no more likely than those with LOD to develop NPS other than apathy, residents with YOD still received psychotropic drugs more often in the treatment of NPS. This underscores the need for appropriate attention to effective non-pharmacological interventions for the management of NPS in YOD.

References

1. Mulders AJMJ, Zuidema SU, Verhey FR, Koopmans RTCM: Characteristics of institutionalized young onset dementia patients – the BEYOnD study. International Psychogeriatrics 2014;12:1973–1981.
2. Mulders AJMJ, Fick IWF, Bor H, et al.: Prevalence and correlates of neuropsychiatric symptoms in nursing home patients with young-onset Dementia: The BEYOnD Study. Journal of the American Medical Directors Association 2016;17:495-500.
3. Murman DLD, Chen Q, Powell MC, et al.: The incremental direct costs associated with behavioral symptoms in AD. Neurology 2002;59:1721-1729.
4. Wetzels R, Zuidema S, de Jonghe JF, Verhey FJ, Koopmans RTCM: Determinants of quality of life in nursing home residents with dementia. Dementia and Geriatric Cognitive Disorders 2010;29:189-197.
5. Zwijsen SA, Kabboord A, Eefsting JA, et al.: Nurses in distress? An explorative study into the relation between distress and individual neuropsychiatric symptoms of people with dementia in nursing homes. International Journal of Geriatric Psychiatry 2014; 29:384-391.
6. Wetzels R, Zuidema SU, Jansen I, Verhey FJ, Koopmans RTCM: Course of neuropsychiatric symptoms in residents with dementia in long-term care institutions: a systematic review. International Psychogeriatrics 2010;22:1040-1053.
7. Brodaty H, Draper BM, Low LF: Behavioural and psychological symptoms of dementia: a seven-tiered model of service delivery. The Medical journal of Australia 2003;178:231-234.
8. Bakker C, de Vugt ME, van Vliet D, et al.: Predictors of the time to institutionalization in young-versus late-onset dementia: results from the needs in young onset dementia (NeedYD) study. Journal of the American Medical Directors Association 2012; 14:248-253.
9. Zuidema SU, de Jonghe JF, Verhey FRJ, Koopmans RCTM: Predictors of neuropsychiatric symptoms in nursing home patients: influence of gender and dementia severity. International Journal of Geriatric Psychiatry 2009;24:1079-1086.
10. Harvey RJ, Skeleton-Robinson M, Rossor MN: The prevalence and causes of dementia in people under the age of 65 years. Journal of neurology, neurosurgery, and psychiatry 2003;74(9):206-1209.
11. Ratnavalli E, Brayne C, Dawson K, Hodges JR: The prevalence of frontotemporal dementia. Neurology 2002;58(11):1615-1621.

12. de Vugt ME, Riedijk SR, Aalten P, et al.: Impact of behavioural problems on spousal caregivers: A comparion between Alzheimer's disease and Frontotemporal Dementia. Dementia Geriatric Cognitive Disorders 2006;22:35-41.

13. Aalten P, Van Valen E, Clare L, Kenny G, Verhey FRJ: Awareness in dementia: A review of clinical correlates. Aging & Mental Health 2005;9:414-22.

14. Nijk RM, Zuidema SU, Koopmans RT: Prevalence and correlates of psychotropic drug use in Dutch nursing-home patients with dementia. International Psychogeriatrics 2009;21:485-493.

15. Wetzels R, Zuidema SU, de Jonghe JF, Verhey FJ, Koopmans RTCM: Prescribing pattern of psychotropic drugs in nursing home residents with dementia. International Psychogeriatrics 2011;23:1249-59.

16. Toyota Y, Ikeda M, Shinagawa S, et al.: Comparison of behavioral and psychological symptoms in early-onset and late-onset Alzheimer's disease. International Journal of Geriatric Psychiatry 2007;22:896-901.

17. van Vliet D, de Vugt ME, Aalten P, et al.: Prevalence of neuropsychiatric symptoms in young onset compared to late-onset Alzheimer's disease - part 1: findings of the two year longitudinal NeedYD-study. Dementia and Geriatric Cognitive Disorders 2012; 34:319-327.

18. Mushtaq R, Pinto C, Tarfarosh SF, et al.: Comparison of the Behavioral and Psychological Symptoms of Dementia (BPSD) in Early-Onset and Late-Onset Alzheimer's Disease: A Study from South East Asia (Kashmir, India). Cureus 2016;8:625.

19. Hori K, Oda T, Asaoka T, et al.: First episodes of behavioral symptoms in Alzheimer's disease patients at age 90 and over, and early-onset Alzheimer's disease: comparison with senile dementia of Alzheimer's type. Psychiatry and Clinical Neurosciences 2005;59:730-735.

20. van Duinen-van den IJssel JCL, Appelhof B, Zwijsen SA, et al.: Behavior and Evolution of Young-ONset Dementia part 2 (BEYOND-II) study: an intervention study aimed at improvement in the management of challenging behavior in institutionalized people with young-onset dementia. International Psychogeriatrics 2017; epub ahead of print.

21. Zwijsen SA, Smalbrugge M, Zuidema SU, et al.: Grip on challenging behaviour: a multidisciplinary care programme for managing behavioural problems in nursing home residents with dementia. Study protocol. BMC Health Services Research 2011; 11:41.

22. American Psychiatric Association: Diagnostic and statistical manual of mental disorders- text revision: DSM-IV-TR. Washington DC, American Psychiatric Association, 2000, vol 1, pp 943.
23. Gorno-Tempini ML, Hillis AE, Weintraub S, et al.: Classification of primary progressive aphasia and its variants. Neurology 2011;76:1006-1014.
24. McKeith IG: Consensus guidelines for the clinical and pathologic diagnosis of dementia with Lewy bodies (DLB): report of the Consortium on DLB International Workshop. Journal of Alzheimer's Disease 2006;9:417-423.
25. McKhann GD, Folstein M, Katzman R, Price D, Standlan EM: Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Healt and Human Services Task Force on Alzheimer's Disease. Neurology 1984;34:939-944.
26. Rascovsky K, Hodges JR, Knopman D, et al.: Sensitivity of revised diagnostic criteria for the behavioural variant of frontotemporal dementia. Brain: a journal of neurology 2011;134:2456-2477.
27. Roman GC, Tatemichi TK, Erkinjuntti T, et al.: Vascular dementia: diagnostic criteria for research studies. Report of the NINDS-AIREN International Workshop. Neurology 1993;43:250-260.
28. Kat MG, de Jonghe JF, Aalten P, et al.: Neuropsychiatric symptoms of dementia: psychometric aspects of the Dutch Neuropsychiatric Inventory (NPI). Tijdschrift voor Gerontologie en Geriatrie 2002;33:150-155.
29. Kaufer DI, Cummings JL, Ketchel P, et al.:Validation of the NPI-Q, a brief clinical form of the Neuropsychiatric Inventory. Journal of Neuropsychiatry and Clinical Neurosciences 2000;12:233-239.
30. Zuidema SU, de Jonghe JF, Verhey FR, Koopmans RCTM: Neuropsychiatric Symptoms in Nursing Home Patients: Factor Structure Invariance of the Dutch Nursing Home Version of the Neuropsychiatric Inventory in Different Stages of Dementia. Dementia and Geriatric Cognitive Disorders 2007;24:169–176.
31. Cohen-Mansfield J, Billig N: Agitated behaviors in the elderly. A conceptual review. Journal of the American Geriatrics Society 1986;34:711–721.
32. de Jonghe JF, Kat MG: Factor structure and validity of the Dutch version of the Cohen Mansfield Agitation Inventory (CMAI-D). Journal of the American Geriatrics Society 1996;44:888-889.
33. Zuidema SU, de Jonghe JF, Verhey F R, Koopmans RCTM: Agitation in Dutch institutionalized patients with dementia: factor analysis of the Dutch version of

the Cohen-Mansfield Agitation Inventory. Dementia and Geriatric Cognitive Disorders 2007;23:35-41.

34. Reisberg B, Ferris SH, de Leon MJ, Crook T: The Global Deterioration Scale for assessment of primary degenerative dementia. The American Journal of Psychiatry 1982;139:1136-1139.

35. Nordic Council on Medicines: Guidelines for ATC Classification, WHO Collaborating Center for Drugs Statistics Methodology: Oslo (Norway), 1997.

36. Cohen-Mansfield J, Libin A:Verbal and physical non-aggressive agitated behaviors in elderly persons with dementia: robustness of syndromes. Journal of Psychiatric Research 2005;39:325-332.

37. Appelhof B, Bakker C, van Duinen-van den IJssel JCL, et al.: The determinants of quality of life of nursing home residents with young-onset dementia and the differences between dementia subtypes. Dementia and geriatric cognitive disorders 2017;43:320–329.

38. Zuidema SU, de Jonghe JF, Verhey FR, Koopmans RCTM: Psychotropic drug prescription in nursing home patients with dementia: influence of environmental correlates and staff distress on physicians' prescription behavior. International Psychogeriatrics 2011;23:1632-1639.


Family
I'm glad I
I love you
I wish I could remember
Pain
New challe
help
happiness
love
love life
how
Take care of the children
I forgot
I don't know
Golden years
enjoy
Good life
Work
learning
why
angry
I have
Friends
to grow
away from home
the beginning

Chapter 4

BEYOND-II STUDY PROTOCOL

Behavior and Evolution of Young ONset Dementia part 2 (BEYOND-II) study: an intervention study aimed at improvement in the management of neuropsychiatric symptoms in institutionalized people with young onset dementia

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Abstract

Background: Both neuropsychiatric symptoms (NPS) and psychotropic drug use are common in institutionalized People with Young Onset Dementia (PwYOD) and can produce negative outcomes such as reduced quality of life and high workload. In community-dwelling PwYOD, NPS are found to be associated with unmet care needs. This emphasizes the importance of a care program for the management of NPS in institutionalized PwYOD that also addresses unmet care needs and psychotropic drug use. The objectives of the Behavior and Evolution of Young ONset Dementia part 2 (BEYOND-II) study are to develop a care program for the management of NPS in institutionalized PwYOD and to evaluate its effectiveness.

Methods: The care program consists of an educational program combined with an intervention to manage NPS with the following five steps: the evaluation of psychotropic drug prescription, detection, analysis (including the detection of unmet needs), treatment and the evaluation of NPS. A stepped wedge design will be used to evaluate its effectiveness. The primary outcomes are agitation and aggression and other NPS. The secondary outcomes are psychotropic drug use, quality of life, the workload of nursing staff and job satisfaction. Additionally, a process analysis and a cost-consequence analysis will be conducted.

Conclusions: The study protocol of the Beyond-II study describes the development, implementation and evaluation of a care program for the management of NPS in institutionalized PwYOD. This care program provides a structured method for the management of NPS, in which unmet needs and psychotropic drug use are also addressed.

Introduction

In approximately 6-9% of all people with dementia the first symptoms develop before the age of 65 [1]. This so-called young onset dementia (YOD) poses challenges that are specifically related to the particular life phase in which the dementia occurs, such as a delay in obtaining a diagnosis and a consequential delay in the initiation of appropriate care and support [2,3]. Furthermore, people with YOD (PwYOD) have specific needs that are frequently unmet; these needs involve day-time activities, social interaction and mobility [4]. In community-dwelling PwYOD these unmet care needs have been found related to the onset of, and increase in neuropsychiatric symptoms (NPS). This finding emphasizes the importance of addressing unmet care needs in care programs for NPS in order to improve the management of these behaviors in PwYOD [4].

NPS such as agitation, apathy or depression are common in PwYOD and can be burdensome for the person with dementia and/or the environment (e.g., nursing staff, informal caregivers, other residents). A recent Dutch study found that 88% of the institutionalized PwYOD showed clinically relevant NPS, with agitation and apathy being the most prevalent symptoms [5,6]. This prevalence rate could be related to the high proportion of people with frontotemporal dementia, in which NPS is the most predominant symptom [5-7]. Furthermore, 50% of institutionalized PwYOD are men, and research shows that extremely NPS and agitated and aggressive behaviors are more likely to occur in men below the age of 70 [8].

NPS in late onset dementia (LOD) are associated with negative health outcomes for the person with dementia as well as for healthcare professionals. These outcomes include reduced quality of life (QoL), increased healthcare costs and increased nursing staff burden [9-12]. These negative health outcomes could also apply to YOD. Moreover, compared to LOD, nurses caring for PwYOD are presumably more often confronted with severe or extreme NPS, especially given the higher prevalence of aggressive behavior in PwYOD [5]. In particular, agitated and aggressive behavior appears to be strongly related to perceived burden [12]. It is likely that these behaviors will increase both the burden and workload of nurses caring for PwYOD and have a negative impact on their feelings of competence. Additionally, it is possible that the impact of NPS lowers the threshold for the use of psychotropic drugs for treatment. Indeed, Mulders et al. (2016) found that in YOD 87.6 % of residents used one or more psychotropic drug(s) [5]. This is concerning because, even though psychotropic drugs can be effective in reducing NPS, they are also associated with negative health outcomes and reduced QoL [11, 13, 14]. Other studies have shown

that non-pharmacological interventions with less adverse effects are also effective in the management of NPS [15-17]. Therefore, the high prevalence rates of NPS and psychotropic drug use (PDU) in institutionalized PwYOD and the negative consequences for residents and nursing staff stresses the importance of the systematic non-pharmacological management of NPS.

The "Grip on challenging behavior" care program has shown effectiveness in the management of NPS in dementia [18, 19]. The Grip care program is based on the generic guidelines for the management of NPS in dementia for the professionals most involved in the care of institutionalized people with dementia: nursing staff, elderly care physicians and psychologists [20-23]. The care program consists of a comprehensive educational program combined with a systematic intervention with the following four steps to manage NPS namely, the detection, analysis, treatment and evaluation. However, this care program is mainly developed for LOD and does not specifically focus on YOD. Therefore, it does not address the possible factors related to a younger age in the management of NPS, such as the different care needs of these younger individuals and the high levels of PDU [4,5]. However, the Grip care program offers a promising starting point for the development of a care program to manage NPS in PwYOD. Furthermore, this care program has proven to be effective in decreasing the prevalence of NPS and PDU and in increasing job satisfaction of the nursing staff [24-25].

Aim and research questions

The Behavior and Evolution of Young ONset Dementia part 2 (BEYOND-II) intervention study aimed to improve the management of NPS in YOD by researching the effects of a newly developed multi-component care program in institutionalized PwYOD. The care program will be based on the 'Grip on challenging behavior' care program. The current paper describes the design of a trial to investigate the effects of the care program, a process evaluation to investigate the implementation of the care program, and a cost-consequence analysis to estimate the monetary value of the care program. Based on previous research on the management of NPS in people with LOD, we expect that the care program will result in a decline in NPS and a decrease in the use of psychotropic drugs.

The research questions are as follows:
(1) What is the effect of the care program on the prevalence and severity of NPS, particularly agitation and aggression, compared to care as usual in YOD Special Care Units (SCUs)?
(2) What is the effect of the care program on PDU and QoL of institutionalized PwYOD?

(3) What is the effect of the care program on nursing staff in terms of workload, absenteeism and job satisfaction?
(3) Was the care program implemented as planned?
(4) What are cost-consequences of the implementation of the care program?

Methods

Development of the care program

The care program in this study is based on the 'Grip on challenging behavior' care program, that consists of an educational program followed by the implementation of four consecutive steps: detection, analysis, treatment and evaluation of NPS. At the start of the implementation of the 'Grip on challenging behavior' care program all staff (nurses, elderly care physicians and psychologists) in the SCU received an educational program that consists of two training sessions in which causes and mechanisms of NPS were discussed and the use of the care program was explained. Six months after implementation all staff received a retraining to enhance implementation of the care program. The 'Grip on challenging behavior' care program is described in detail elsewhere [18].

The educational program was tailored by the researchers to the specific (clinical) characteristics and context of YOD. In the Netherlands, nurses are generally only educated in dementia care which does not cover YOD specific issues. The educational program was adapted in consultation with health care psychologists and elderly care physicians working in YOD SCUs. The adapted educational program for the SCU staff covers YOD in general as well as factors influencing the occurrence and persistence of NPS in YOD and the (steps of the) care program.

The four steps of the 'Grip on challenging behavior' care program remained the same. However, the evaluation of appropriateness of psychotropic drug prescription was added to the care program as a separate step and also a tool for the detection of unmet needs was added to the analysis step of the care program. The tool for the evaluation of appropriateness of psychotropic drug prescription is based on the Appropriateness of Psychotropic Drug Prescription In Dementia (APID)-instrument [26-27]. The APID is a research tool for evaluating the appropriateness of psychotropic drug prescription prescribed for NPS in patients with dementia in nursing homes. The APID tool was transformed into a self-evaluation tool for use by the elderly care physician. This was done in consultation with the developers of the APID-instrument. A pilot was held in the LOD

SCUs of two nursing homes. The results from the pilot were then discussed in a consensus meeting with the developers of the APID-instrument. The tool for the evaluation of appropriateness of the psychotropic drug prescription was adapted based on the results of this consensus meeting.

The tool for the detection of unmet needs is based on the Dutch version of the Camberwell Assessment of Need for the Elderly (CANE) [28-29]. The CANE is a semi-structured interview that covers the needs of people with dementia. Panel group discussions with health care professionals and researchers with experience working with PwYOD were used to adapt the CANE to the specific areas of needs of institutionalized PwYOD. Additionally, the assessment of the CANE was adapted for observational use, allowing for use and interpretation by nurses as a part of the care program. A pilot study was held in a YOD SCU that did not participate in the overall study. The usability of the tool was evaluated using semi-structured qualitative interviews with nurses, PwYOD residing in the SCU, and informal caregivers. The tool for the detection of unmet needs was adapted based on the results of this pilot.

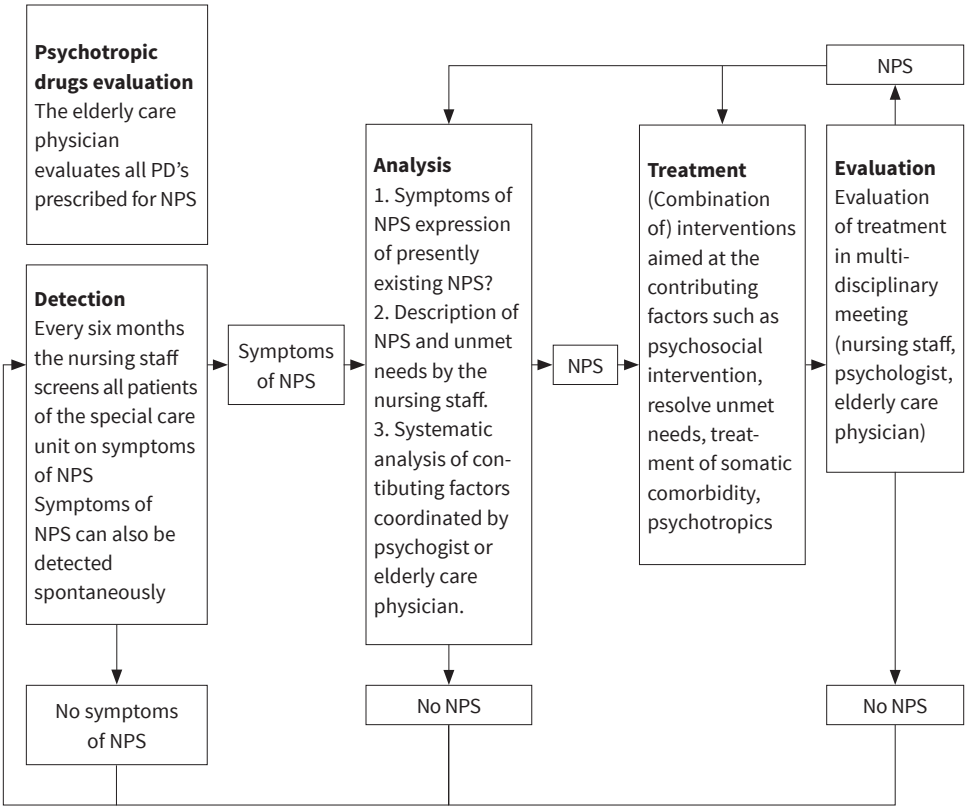
The 'Grip on challenging behavior' care program was originally on paper. Currently, in most Dutch nursing homes electronic client files are used. Therefore, the care program is fully digitalized. All elements of the care program are integrated in a web based environment which makes it possible for the SCU team to have direct access to the care program. Also automated notifications can be sent to all involved disciplines.

Intervention

After the above mentioned adaptations, the intervention offered to the SCUs consists of an educational program followed by the implementation of the five-step care program on the management of NPS. The steps of the care program are described in Figure 1. The first step of the care program is the evaluation of appropriateness of psychotropic drug prescription. This is a separate step, the other four steps are consecutive and form a cycle. This step involves using the tool for the evaluation of appropriateness of psychotropic drug prescription. This will be completed for all residents by the elderly care physician in the first two months after the SCU is enrolled in the intervention condition. After the initial screening, the elderly care physician can consider psychotropic drug prescription monitoring with the self-evaluation tool at his own discretion. Detection of NPS, can occur in usual (daily) observations or with the screening tool for the detection of NPS. Residents are systematically screened every six months for NPS by the nurses with the screening tool as part of the care program. After detection, (symptoms of) NPS are *analyzed* by the

nurses. The *analysis* contains questions about the behavior (e.g., describe the behavior, describe the frequency) and includes the tool for the detection of unmet needs in order to investigate whether unmet needs could be a cause of NPS. If necessary, the elderly care physician or psychologist continues the analysis. The outcome of the analysis is discussed in multidisciplinary meetings. After the analysis, the options for treatment are discussed, and the *treatment* plan is established. The treatment plan contains a specifically defined, measurable treatment goal. Psychosocial treatments are preferred; psychotropic drugs are prescribed only if psychological treatment has little or no effect. The last step is the *evaluation* of the treatment. The frequency and severity of NPS before and after treatment are compared. When treatment outcomes are unsatisfactory, other treatments are considered, or the analysis is performed again.

Figure 1. The five steps of the care program 'Grip on NPS in institutionalized PwYOD'.



NPS = neuropsychiatric symptoms; PD's= Psychotropic Drugs

Design

A stepped wedge design (Table 1) will be used to evaluate the effectiveness of the care program. This design allows clusters (in this case, YOD SCUs) to cross-over from a control to an intervention condition over time and assures that all clusters receive the care program and can benefit from the possible positive effects of the intervention [30]. This increases the motivation of care organizations to participate in the study. Also, a stepped wedge design is considered appropriate when there are practical and logistic constraints to implementing the intervention simultaneously to all participants in the intervention condition, which is applicable to this study [30]. Moreover, a stepped wedge design increases the study power by enabling analyses between and within groups [31]. In this study, YOD SCUs from nursing homes throughout the Netherlands will be included. The YOD-SCUs will be randomly assigned to one of three groups. There will be four assessments at six month intervals during a period of 18 months. After each assessment, a new group will enter the intervention condition. The control condition will consist of care as usual without the educational program and use of the care program.

Table 1. Stepped wedge design

	Cluster 1	Cluster 2	Cluster 3
T0	0	0	0
T1	1	0	0
T2	1	1	0
T3	1	1	1

0 = control condition; 1= intervention condition

There are four, half yearly, assessments. Each cluster consists of four or five YOD-SCUs

Participants

Eligible YOD SCUs will be recruited through nursing homes that are affiliated with the Dutch YOD Knowledge Center (DKC). PwYOD who have a diagnosis of dementia with symptom onset before the age of 65 and who have been residing in the SCU for at least one month will be included in the study. Diagnoses of dementia subtype will be made according to the regular criteria and retrieved from the medical file [32-37]. People with dementia caused by human immunodeficiency virus (HIV), traumatic brain injury, Down syndrome, Korsakov or Huntington's disease will be excluded. All nurses employed in the YOD SCU will be included in the study.

Power calculation

In the power calculation, a 6.8 decrease in NPS as measured with the Cohen-Mansfield Agitation Inventory (CMAI) is considered a clinically relevant effect of the care program. This value corresponds to the 0.4 SD of the CMAI (mean 48.8 (16.7)) of the Beyond-I study [6]. We assume an ICC of 0.1, which is based on a Dutch study of institutionalized people with LOD [38]. Based on these assumptions, a significance level (alpha) of 0.05 and a power (beta) of 0.80, 10 YOD SCUs with 20 people each in three groups with four measurements are needed for this study. No further attrition is expected because newly admitted residents will replace those who are discharged or die during the study. However, it is possible that an SCU will drop out, for example, due to relocation or organizational problems. Therefore, 13 YOD SCUs will be recruited.

Outcome measures

Primary outcomes

Agitation and aggression will be assessed with the Dutch version of the Cohen-Mansfield Agitation Inventory (CMAI-D) [39,40]. The CMAI is the only instrument that specifically addresses agitation and aggression that has been translated into Dutch and has well-established validity and reliability [40, 41]. The CMAI-D assesses 29 agitated or aggressive behaviors. The frequency of each symptom is rated on a seven-point Likert-scale (1-7) ranging from never to several times an hour. A total sum score (range 29-203) can be calculated as well as a score for the subscales of physically nonaggressive behavior, physically aggressive behavior and verbally agitated behavior [42].

Other NPS will be assessed with the Dutch version of the Neuropsychiatric Inventory-Nursing Home version (NPI-NH) [43-44]. The NPI-NH has a high-interrater reliability and has been found to be a valid measure for NPS [43]. The NPI-NH contains twelve neuropsychiatric symptoms. For each symptom, a screening question will be used to determine whether the symptom is present. For each symptom, Severity (S) and Frequency (F) will be rated on three-point (1-3) and four-point (1-4) Likert-scales, respectively. Additionally, the occupational disruptiveness of symptoms will be assessed on a six-point Likert-scale ranging from no distress to extreme distress (0-5). Scores for each symptom are calculated as F multiplied by S (range 1-12), and a total score can be calculated by summing the FxS scores ranging from 0 (symptom was absent) to 144. A total score for occupational disruptiveness can be calculated by adding each score (range 0-60). For an overview of all measurements, see Table 2.

Secondary outcomes: institutionalized PwYOD

QoL will be assessed with the Quality of Life in Dementia (QUALIDEM) questionnaire [45,46]. The Qualidem is a 37-item behavior observation scale for people with dementia in residential care. Nursing staff rate the Qol for the PwYOD over the preceding week on a four-point scale, ranging from never to almost daily. The Qualidem has nine subscales: care relationship, positive affect, negative affect, restless tense behavior, positive self-image, social relations, social isolation, feeling at home and having something to do.

Dementia severity will be assessed with the Global Deterioration Scale (GDS) [47]. The GDS is a validated seven-point scale that describes seven different stages of dementia ranging from 'no impairment' to 'very severe cognitive impairment'.

PDU will be derived from the nursing home pharmacist's electronic registration system and will be classified according to the Anatomical Therapeutic Chemical (ATC) classification system into groups of antipsychotics, anxiolytics, hypnotics, antidepressants, antiepileptic drugs and cholinesterase inhibitors [48].

Secondary outcomes: nursing staff

Workload will be assessed with the Dutch version of the Maslach Burnout Inventory, known as the Utrecht Burnout Scale (UBOS) [49,50]. The UBOS is a 20-item questionnaire assessing three components of burnout: emotional exhaustion, depersonalization and decreased personal accomplishment. Questions will be answered on a seven-point scale ranging from 'never' to 'always'.

Job satisfaction and job demands will be assessed with two subscales of the Leiden Quality of Work Questionnaire (LQWQ) [51]. The LQWQ assesses the nursing staff's perception on their quality of work. The two subscales assess 'job satisfaction' and 'job demands' with six and seven items, respectively. Questions are answered on a four-point Likert scale ranging from 'totally disagree' to 'totally agree'.

The staffs attitude towards dementia and dementia care will be assessed with the Approaches to Dementia Questionnaire (ADQ) [52].

Other PwYOD and nursing staff characteristics

The sex, age, and length of stay of the resident will be obtained from the medical file. The age, sex, years of working experience, educational level, and weekly working hours of the nursing staff will also be assessed through a questionnaire. Additionally, staff absenteeism will be obtained from periodical registrations done by the Human Resources department of the nursing home.

Special care unit characteristics

Characteristics of the SCU will be registered, including the care concept used at the SCU, the living environment (small scale/ traditional long term care) and the nursing staff-resident ratio. This will be completed through structured telephonic interviews with the site coordinator of the study.

Table 2. Flowchart of measures used during the assessments

Outcome measure	**Operationalization (Type of instrument)**	**Time of assessment**				
PwYOD		**S**	**T0**	**T1**	**T2**	**T3**
Primary outcome						
Agitation and aggression	CMAI-D[a] (SI)		f	f	f	f
Frequency and severity of neuropsychiatric symptoms	NPI-NH[b] (SI)		f	f	f	f
Secondary outcome						
Quality of life	Qualidem[c] (SI)		f	f	f	f
Severity of dementia	GDS[d] (RS)		f	f	f	f
Psychotropic drug use	ATC code, dose, frequency		f	f	f	f
Additional variables						
Inclusion/ exclusion criteria		ecp/p	ecp/p	ecp/p	ecp/p	ecp/p
Demographic data	Age, sex, length of stay		f	f	f	f
Medical record investigation	Current dementia diagnosis, comorbidity		f	f*	f*	f*
Nursing staff						
Secondary outcome						
Workload	UBOS[e] (Q)		n	n	n	n

Table 2 (no. 66) continued

Job satisfaction	'Job satisfaction' and 'Work/time pressure' of the Leiden Quality of Work Questionnaire [f](Q)	n	n	n	n
Absence rate	Periodical registrations of the NH personnel departments	e	e	e	e
Additional variables					
Nursing staff attitude	ADQ[g] (Q)	n	n	n	n
Demographic data	Age, sex, educational level, years of working experience	n	n	n	n
YOD SCU					
Care concept	Three item questionnaire on the extent to which a specific care concept is implemented at the SCU (SI)	e	e	e	e
Nursing staff/ resident ratio		e	e	e	e
Living environment		e			e

[a](Cohen-Mansfield et al., 1989)

[b](Wood et al., 2000)

[c](Ettema et al., 2007a; b)

[d](Reisberg et al., 1982)

[e](Maslach, 1986)

[f](Van der Doef and Maes, 1999)

[g](Lintern, 2001a)

S = Screening; T0-T3 = measurements 0-3; SI = Structured Interview; RS = Rating Scale; Q = questionnaire; f = informant is first responsible nurse; ecp = informant is elderly care physician; p = informant is psychologist; n = informant is nurse; e = informant is manager or employee of personnel department of the nursing home.

Ethical considerations

The study protocol has been approved by the Medical Ethics Committee region Arnhem/ Nijmegen (file nr: 2015-1558). This research project will be completed according to the principles of the Declaration of Helsinki (version November 2013, www.wma.net). Written informed consent will be obtained from the legal representative of each resident, and all data will be anonymized.

Procedures

Information on the inclusion and exclusion criteria will be sent to the participating YOD-SCUs. Only the legal representatives of institutionalized PwYOD who meet the inclusion criteria will receive written information and will be asked for their informed consent to participate. Informed consent will be requested for information retrieval from the medical file and for proxy assessments. After written informed consent is received, the researchers will contact the nursing staff to arrange the assessment interview. All resident outcomes will be assessed through interviews with the nursing staff. Respondents will be considered reliable if they are the vocational nurse specifically assigned to the resident or have had regular contact with the resident in the past month. No interviews will be held with the PwYOD themselves. Trained researchers and research assistants will collect the data through structured interviews with the nursing staff and from the resident's medical files. The nurses from the participating SCUs will be aware that they are in the intervention condition, because that condition requires working with the care program. Therefore, it is not possible to blind the nurses, researchers or research assistants. No feedback will be given to the nurses during the assessments regarding the scores on the outcomes measures.

Data Analysis

Data entry of the PwYOD and nursing staff outcomes will be performed in Project Manager Internet Server (ProMISe), a web-based data management system. All entered data will be checked to safeguard data entry. For the primary research question, the CMAI- score and the NPI-NH score will be used as outcomes. Age, sex, length of stay, dementia severity, and prescription of antipsychotics and other psychotropic drugs will be used as covariates. QoL (Qualidem), burnout (UBOS), job satisfaction (LQWQ), and job demands (LQWQ) scores will be used as secondary outcomes. Nurses age, sex, years of working experience, educational level, and the nurse-resident ratio will be used as covariates. The primary and secondary outcomes will be analyzed using multilevel linear regression and multilevel

logistic regression analyses. These analyses will calculate the effects of the care program on NPS, QoL, the prescription rate of psychotropic drugs, and the workload and job satisfaction of nursing staff.

Process evaluation

A process evaluation will be carried out during the study, using the framework of first- and second-order process data as described by Leontjevas *et al.*(2012) [53]. First-order process data will be used for interpretation of the effect of the care program. This entails sampling quality (external validity) and intervention quality (internal validity). Sampling quality will be determined by (1) the recruitment and randomization procedure for the SCU, (2) the recruitment procedure of the PwYOD, and (3) the reach of the intervention (the proportion of SCU care staff participating in the care program). Intervention quality will be determined by (1) the relevance and feasibility of the care program and (2) the extent to which the program was performed. Second-order data will contain information about the delivered and received implementation components and the barriers and facilitators of the implementation process. These data will be evaluated using structured questionnaires and interviews with primary nurses, team leaders, psychologists and elderly care physicians.

Economic evaluation

A cost-consequences approach (CCA) will be used to estimate the monetary value of the care program. This method provides the most comprehensive presentation of information describing the value of an intervention and is also conceptually the simplest [54].
The impact of the care program on resource use, costs and health outcomes will be estimated on the SCU and resident levels using a balance-sheet approach. Costs will include the following direct costs: (1) costs on the SCU level (time allocated for implementation of the care program); (2) cost of care per resident; and (3) PDU costs. Costs will also include indirect costs associated with staff absenteeism. The time needed for the educational program will be registered separately. Effects of the care program will include: agitation and aggression (assessed with the CMAI), QoL (assessed with the Qualidem), PDU of the PwYOD, and occupational disruptiveness of NPS for the nursing staff.

Discussion

The current paper describes the study design of an interventional study that addresses the management of NPS in YOD, known as the Beyond-II study. To our knowledge, this is the first study that addresses the management of NPS in institutionalized PwYOD. The focus of this study is on the (process) evaluation of the effectiveness and the costs and consequences of the implementation of a newly developed multi-component care program on the management of NPS in institutionalized PwYOD. We expect that the implementation of the care program will result in decreases in NPS and PDU. Implementation is also expected to result in higher job satisfaction among nursing staff.

This study will contribute to the knowledge of the management of NPS in YOD, the mechanisms involved in the management of NPS, and implementation knowledge of care programs in nursing homes. A stepped wedge design will be used in this study to ensure that all participating YOD SCUs can benefit from the care program. Despite the many positive aspects of this study, there are some limitations that have to be considered. Selection bias could be a factor in our study. Although our participating YOD SCUs are recruited from all geographical regions of the Netherlands and are likely to represent the Dutch YOD nursing home population, selection bias may occur because all participating nursing homes are affiliated with the Dutch YOD Knowledge Center. This may be a different group than the YOD nursing homes that are not affiliated with the Dutch YOD Knowledge Center. Another limitation is that informed consent will be obtained for all PwYOD and it is possible that the group for which consent is obtained will be different from the group for which consent cannot be obtained.

Despite these limitations, the stepped wedge design and assessment measures seem appropriate for this study and outweigh the few limitations. The described care program offers the YOD-SCU staff tools for the management of NPS in YOD.

References

1. World Health Organization: Dementia: A Public Health Priority, World Health Organization, 2012.
2. Draper B, Cations M, White F, et al.: Time to diagnosis in young-onset dementia and its determinants: the INSPIRED study. International Journal of Geriatric Psychiatry 2016;11:1217-1224.
3. Van Vliet D, de Vugt ME, Bakker C, et al.: Time to diagnosis in young-onset dementia as compared with late-onset dementia. Psychol Med 2013;43:423-432.
4. Bakker C, de Vugt ME, van Vliet D, et al.: The relationship between unmet care needs in young-onset dementia and the course of neuropsychiatric symptomps: a two year follow-up study. International Psychogeriatrics 2014;26(12):1991–2000.
5. Mulders AJMJ, Fick IWF, Bor H, et al.: Prevalence and correlates of neuropsychiatric symptoms in nursing home patients with young-onset Dementia: The BEYOnD Study. Journal of the American Medical Directors Association 2016;17(6):495-500.
6. Mulders AJMJ, Zuidema SU, Verhey FR, Koopmans RTCM: Characteristics of institutionalized young onset dementia patients – the beyond study. International Psychogeriatrics 2014;12:1973–1981.
7. Rossor MN, Fox NC, Mummery CJ, Schott JM, Warren JD: The diagnosis of young onset dementia. Lancet Neurology 2010;9:793-806.
8. Brodaty H, Draper BM, Low LF: Behavioural and psychological symptoms of dementia: a seven-tiered model of service delivery. The Medical journal of Australia 2003; 178:231-234.
9. Gauthier S, Cummings J, Ballard C, et al.: Management of behavioral problems in Alzheimer's disease. International Psychogeriatrics 2010;22:346–372.
10. Murman DL, Chen Q, Powell MC, et al.: The incremental direct costs associated with behavioral symptoms in AD. Neurology 2002;59(11):1721-1729.
11. Wetzels R, Zuidema SU, de Jonghe J, Verhey F, Koopmans RTCM, et al.: Determinants of quality of life in nursing home residents with dementia. Dement Geriatr Cogn Disord 2010;29(3):189-197.
12. Zwijsen SA, Kabboord A, Eefsting JA, et al.: Nurses in distress? An explorative study into the relation between distress and individual neuropsychiatric symptoms of people with dementia in nursing homes. International Journal of Geriatric Psychiatry 2014; 29(4):384-91.
13. Ballard C, Howard R: Neuroleptic drugs in dementia: benefits and harm. Nature Reviews Neuroscience 2006;7(6):492-500.

14. Schneider LS, Dagerman K, Insel PS: Efficacy and adverse effects of atypical antipsychotics for dementia: meta-analysis of randomized, placebo-controlled trials. American Journal of Geriatric Psychiatry 2006;14:191-210.

15. Cohen-Mansfield J, Libin A, Marx MS: Nonpharmacological treatment of agitation: a controlled trial of systematic individualized intervention. Journals of Gerontology: Series A 2007;62:908-916.

16. Davison TE, Hudgson C, McCabe MP, George K, Buchanan G: An individualized psychosocial approach for "treatment resistant" behavioral symptoms of dementia among aged care residents. International Psychogeriatrics 2007;19:859-873.

17. Livingston G, Johnston K, Katona C, Paton J, Lyketsos CG: Systematic review of psychological approaches to the management of neuropsychiatric symptoms of dementia. American Journal of Psychiatry 2005;162:1996-2021.

18. Zwijsen SA, Gerritsen DL, Eefsting JA, et al.: The development of the Grip on Challenging Behaviour dementia care programme. International Journal Palliative Nursing 2014;20:15-21.

19. Zwijsen SA, Smalbrugge M, Zuidema SU, et al.: Grip on challenging behaviour: a multidisciplinary care programme for managing behavioural problems in nursing home residents with dementia. Study protocol. BMC Health Services Research 2011;11(41): 1-6.

20. Koopmans RTCM, Lavrijsen JC, Hoek JF, Went PB, Schols JM: Dutch elderly care physician: a new generation of nursing home physician specialists. Journal of the American Geriatrics Society 2010;58:1807-1809.

21. Nederlands Instituut van Psychologen (NIP): Handreiking Psychologische hulpverlening bij gedragsproblemen bij dementie, Amsterdam, NIP, SPO, 2013.

22. Verenso: Richtlijn Probleemgedrag - met herziene medicatieparagraaf, Utrecht, Verenso, 2008.

23. Verpleegkundigen & Verzorgenden Nederland (V&VN): Richtlijn omgaan met gedragsproblemen bij patiënten met dementie, Nijmegen, V&VN, 2005.

24. Zwijsen SA, Gerritsen DL, Eefsting JA: Coming to grips with challenging behaviour: a cluster randomised controlled trial on the effects of a new care programme for challenging behaviour on burnout, job satisfaction and job demands of care staff on dementia special care units. Int J Nurs Stud 2015;52:68-74.

25. Zwijsen SA, Smalbrugge M, Eefsting J, et al.: Coming to grips with challenging behavior: a cluster randomized controlled trial on the effects of a multidisciplinary care program for challenging behavior in dementia. Journal of the American Medical Directors Association 2014;15(7):531.e1-531.e10.

26. van der Spek K, Gerritsen DL, Smalbrugge M, et al.: PROPER I: frequency and appropriateness of psychotropic drugs use in nursing home patients and its associations: a study protocol. BMC Psychiatry 2013;13:1-7.
27. van der Spek K, Gerritsen DL, Smalbrugge M, et al.: A reliable and valid index was developed to measure appropriate psychotropic drug use in dementia. Journal of Clinical Epidemiology 2015;68(8):903-912.
28. Orrell M, Hancock G: CANE: Camberwell Assessment of Need for the Elderly, Gaskell, 2004.
29. Reynolds T, Thornicroft G, Abas M, et al.: Camberwell Assessment of Need for the Elderly (CANE); development, validity, and reliability. Britisch Journal of Psychiatry 2000;176:444-452.
30. Brown CA, Lilford RJ: The stepped wedge trial design: a systematic review. BMC Medical Research Methodology 2006;6:54.
31. Hussey MA, Hughes JP: Design and analysis of stepped wedge cluster randomized trials. Contemp Clin Trials 2007;28:182-191.
32. American Psychiatric Association: Diagnostic and statistical manual of mental disorders- text revision: DSM-IV-TR. Washington DC, American Psychiatric Association, 2000, vol 1, pp 943.
33. Gorno-Tempini ML, Hillis AE, Weintraub S, et al.: Classification of primary progressive aphasia and its variants. Neurology 2011;76:1006-1014.
34. McKeith IG: Consensus guidelines for the clinical and pathologic diagnosis of dementia with lewy bodies (dlb): Report of the consortium on dlb international workshop. Journal of Alzheimer's Disease 2006;9:417-423.
35. McKhann G, Drachman D, Folstein M, et al.: Clinical diagnosis of alzheimer's disease: Report of the nincds-adrda work group under the auspices of department of health and human services task force on alzheimer's disease. Neurology 1984;34:939 944.
36. Rascovsky K, Hodges JR, Knopman D, et al.: Sensitivity of revised diagnostic criteria for the behavioural variant of frontotemporal dementia. Brain : a journal of neurology 2011;134:2456-2477.
37. Roman GC, Tatemichi TK, Erkinjuntti T, et al.: Vascular dementia: Diagnostic criteria for research studies. Report of the ninds-airen international workshop. Neurology 1993;43:250-260.
38. Zuidema SU, de Jonghe JF, Verhey FR, Koopmans RTCM: Environmental correlates of neuropsychiatric symptoms in nursing home patients with dementia. International Journal of Geriatric Psychiatry 2010;25:14-22.

39. Cohen-Mansfield J, Marx MS, Rosenthal AS: A description of agitation in a nursing home. J Gerontol 1989:44:M77-84.

40. de Jonghe JF, Kat MG: Factor structure and validity of the Dutch version of the Cohen Mansfield Agitation Inventory (CMAI-D). Journal of the American Geriatrics Society 1996;44:888-889.

41. Zuidema SU, Buursema LA, Gerritsen MG, et al: Assessing neuropsychiatric symptoms in nursing home patients with dementia: reliability and reliable change index of the Neuropsychiatric Inventory and the Cohen-Mansfield Agitation Inventory. International Journal of Geriatric Psychiatry 2011:26;127-134.

42. Zuidema SU, de Jonghe JF, Verhey FR, Koopmans RCTM: Agitation in Dutch institutionalized patients with dementia: factor analysis of the Dutch version of the Cohen-Mansfield Agitation Inventory. Dementia and Geriatric Cognitive Disorders 2007;23:35-41.

43. Kat MG, de Jonghe JF, Aalten P, et al.: Neuropsychiatric symptoms of dementia: Psychometric aspects of the dutch neuropsychiatric inventory (npi). Tijdschrift voor Gerontologie en Geriatrie 2002;33:150-155.

44. Wood S, Cummings EL, Hsu MA, et al.: The use of the neuropsychiatric inventory in nursing home residents. Characterization and measurement. American Journal of Geriatric Psychiatry 2000;8:75-83.

45. Ettema TP, Droes RM, de Lange J, Mellenbergh GJ, Ribbe MW: Qualidem: Development and evaluation of a dementia specific quality of life instrument. Scalability, reliability and internal structure. Int J Geriatr Psychiatry 2007;22:549-556.

46. Ettema TP, Droes RM, de Lange J, Mellenbergh GJ, Ribbe MW: QUALIDEM: development and evaluation of a dementia-specific quality of life instrument –validation. International Journal of Geriatric Psychiatry 2007;22:424–430.

47. Reisberg B, Ferris SH, de Leon MJ, Crook T: The global deterioration scale for assessment of primary degenerative dementia. The American Journal of Psychiatry 1982;139:1136–1139.

48. WHO: Anatomical therapeutical chemical (atc) classification index including defined daily doses (ddds) for plain substances. Oslo, World Health Organisation Collaborating Centre for Drug Statistics Methodology, 1997.

49. Maslach C, Jackson SE: The Maslach Burnout Inventory Manual. Palo Alto, CA: Consulting Psychology Press, Inc, 1986.

50. Schaufeli W, Van Dierendonck D: UBOS, Utrecht Burnout Scale: Manual. Zeist SWETS Test Publishers, 2000.

51. Van der Doef M, Maes S: The Leiden quality of work questionnaire: its construction, factor structure, and psychometric qualities. Psychological Reports 1999;85:963-970.

52. Lintern T: Quality in Dementia Care: Evaluating Staff Attitudes and Behaviour. University of wales, Bangor, 2001.

53. Leontjevas R, Gerritsen DL, Koopmans RTCM, Smalbrugge M, Vernooij-Dassen MJ: Process evaluation to explore internal and external validity of the "Act in Case of Depression" care program in nursing homes. Journal of the American Medical Directors Association 2012;13:448e481-448e488.

54. Mauskopf JA, Paul JE, Grant DM, Stergachis A: The role of cost-consequence analysis in healthcare decision-making. Pharmacoeconomics 1998;13:277-288.


Family
I'm glad I
I love you
I wish I could remember
Pain
New challe
help
happiness
love
love life
how
Take care of the children
I forgot
I don't know
Golden years
enjoy
Good life
Work
learning
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angry
I have
Friends
to grow
away from home
the beginning

Chapter 5

BEYOND-II STUDY PROCESS EVALUATION

Process evaluation of an intervention for the management of neuropsychiatric symptoms in young-onset dementia

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Abstract

Background: An intervention for the management of neuropsychiatric symptoms in institutionalized people with young-onset dementia was implemented in care units delivering specialized treatment and support for younger people with dementia.
Objectives: Data about sample quality and intervention quality was evaluated in order to better understand internal and external validity. In addition, data about the implementation strategy and factors affecting implementation were evaluated to improve further implementation of the intervention.
Setting: Dutch long-term care facilities providing specialized care for young-onset dementia.
Measurements: A description of the recruitment, randomization procedure, and intervention reach was carried out in order to determine sample quality. To determine intervention quality data on satisfaction, relevance, feasibility, and fidelity was collected through a questionnaire and reports logged on the server of the web-based intervention. A description of the implementation strategy was provided. Barriers and facilitators for implementation were collected by a questionnaire and analyzed by deductive content analysis.
Results: Care units varied in size and were recruited from different geographical regions in the Netherlands. The informed consent rate of the residents was 87.7%. The majority of the nursing home staff was satisfied with the intervention. However, parts of the intervention were perceived as less relevant for the own organization. The feasibility of the intervention was considered low. The fidelity differed between care units. The implementation strategy did not overcome all barriers. Factors effecting implementation covered three themes: organizational aspects, culture of the organization, and aspects of the intervention.
Conclusions: In general, our results showed sufficient internal and external validity warranting further effect analyses. Adaptations to specific steps of the care program should be considered to increase feasibility and sustainability. In addition, integration of the care program into the electronic health records is expected to further improve implementation.

Introduction

In institutionalized people with young-onset dementia (YOD), neuropsychiatric symptoms (NPS) are highly prevalent [1,2]. NPS have been associated with negative health outcomes like a loss of quality of life, increased cost of care, and a high workload for nursing home (NH) staff [3-5]. Psychotropic drugs are often used in the treatment of NPS in institutionalized people with YOD [1], which are negatively associated with quality of life in both YOD and LOD [3,6-8]. Therefore, in the Behavior and Evolution of Young-ONset Dementia part 2 (Beyond-II) study, an intervention for the management of NPS in YOD was implemented on long-term care units offering specialized treatment and support in YOD [9].

A randomized controlled trial (RCT) was conducted to evaluate the effect of the intervention on the prevalence of NPS and psychotropic drug use (PDU) in NH residents with YOD, and workload, absenteeism, and job satisfaction of the NH staff [9]. In order to interpret the outcomes of the RCT, information about internal and external validity is important [10]. Internal validity refers to the extent to which effects are a result of the intervention [11]. For example, a RCT could fail to find an effect of a potential successful intervention due to too small sample sizes [11]. External validity refers to the generalizability of the effects of the intervention [11]. For instance, if recruitment rates are low, the research population might not be representative of a wider population.

Besides information on validity, a better understanding of the implementation process is necessary to understand why the intervention was or was not effective and how to improve sustainability in clinical practice [10, 12, 13]. A recent editorial stated that due to consequences of practical difficulties in conducting applied research in the context of daily practice, it is naïve to expect that complex intervention in NHs are always completely carried out as planned [14]. Therefore, potential successful interventions might fail to show effect, because they were not delivered as indented [12, 15-17]. This is expressed as low treatment fidelity [12,17]. In order to allow for conclusions about the effectiveness of the intervention in clinical practice, it is important to understand the relationship between contextual factors and the effectiveness of the intervention, rather than trying to control for contextual influences [13, 16]. This context consists of all factors, external to the intervention, which might facilitate or hinder implementation [17]. Previous implementation studies in NHs already reported on contextual barriers for implementation like staff turnover, staff shortage, low staff motivation, lack of leadership, absence of management support, and organizational changes [18-20]. In order to try to overcome these contextual barriers and increase effectiveness of our intervention, an implementation strategy was

developed alongside the intervention. Reporting on the used implementation strategy and how it was received is important as it provide future users of the intervention with vital information about how to reproduce the intervention [10, 17, 21].

A process evaluation provides knowledge on validity and implementation [10]. Therefore, in this study, a process evaluation was performed for an intervention aimed at improvement of the management of NPS in institutionalized people with YOD (1) to establish internal and external validity, and (2) to provide information about the implementation strategy and factors affecting implementation.

Methods

This process evaluation is part of the Beyond-II study and was conducted before effect analysis of the intervention. The design of the Beyond-II study and information about the development of the intervention are described in full detail elsewhere [9, 22].

Intervention

The intervention in this study is based on the "Grip on challenging behavior" care program [22, 23]. After implementation of this care program in late-onset dementia (LOD), a decrease in NPS and PDU, and an increase in job satisfaction of the NH staff was found [24, 25]. The care program provided guidance for the multidisciplinary team involved in the management of NPS in Dutch NHs (nursing staff, specially trained elderly care physicians and psychologists) [26, 27] to structure the process of detection, analysis, treatment, and evaluation of NPS (Figure 1). NPS could be every form of behavior that is perceived as challenging by the NH resident or by people surrounding the residents (like NH staff, relatives, other residents), encompassing various symptoms including affective symptoms, such as depression, anxiety and apathy, and behavioral symptoms like aggression, agitation, disinhibition, delusions, and hallucinations.

The steps of the care program were consecutive and formed a cycle, except for the evaluation of appropriateness of psychotropic drug prescription which was a separate step (Figure 1). The first step of the care program was detection of NPS. This occurred through usual observations of the multidisciplinary team or with the use of a screening tool every six months by a vocational nurse. The screening tool was based on the Neuropsychiatric Inventory–Questionnaire (NPI-Q) [28]. After NPS were detected, a structured analysis of the NPS was conducted by the vocational nurse. The analysis contained questions regarding

the time and place of occurrence of the NPS, possible causes, and actions already undertaken by the care staff. In addition, a tool for the detection of unmet needs possibly underling the NPS was used by the vocational nurse. The tool was adapted and extended based on the Dutch version of the Camberwell Assessment of Need for the Elderly (CANE) [29, 30]. When necessary, the physician and/or the psychologist continued the analysis. Their analyses consisted of a checklist to rule out physical or psychiatric causes (physician) or a functional analysis of the NPS (psychologist). After the analysis of the clinician, treatment options were discussed within the multidisciplinary team and a treatment plan was established by a clinician (psychologist or physician). The treatment plan contained a specifically defined, measurable treatment goal. The care program did not prescribe a specific intervention. The choice of the intervention relied on the hypothesized causes of the NPS, the preferences of the resident, and the available options in the NH. However, in accordance with the guidelines on the management of NPS [31-33], psychosocial treatments were preferred; PDU only if other treatment had little or no effect. Treatment outcomes were evaluated by the multidisciplinary team. The frequency and severity of NPS before and after treatment were compared and if unsatisfactory, other treatments were considered or the analysis was performed again.

In a separate step of the care program, the physician used a tool for the evaluation of appropriateness of psychotropic drug prescription within the first two months after implementation for all residents (with our without NPS). The tool was adapted and extended based on the Appropriateness of Psychotropic Drug Prescription In Dementia (APID)-instrument [34, 35]. After this initial screening, the tool was used at the physician's own discretion.

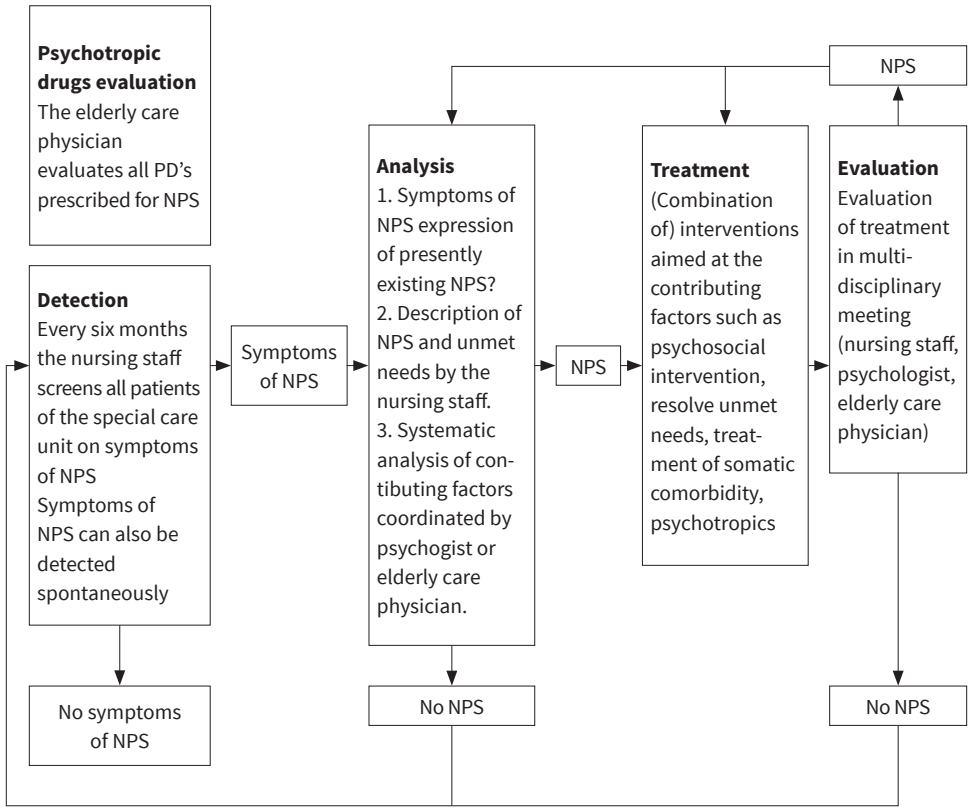

Figure 1. The five steps of the care program 'Grip on NPS in institutionalized people with YOD [9].

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NPS = Neuropsychiatric Symptoms; YOD = young-onset dementia; PD's = Psychotropic Drugs.

Process evaluation model

Previous NH intervention studies successfully used a model proposed by Leontjevas and colleagues, following the framework of Linnan and Steckler [10, 18, 36]. In line with this model, first-order process evaluation data consisting of sample quality and intervention quality is evaluated in order to better understand internal and external validity. In addition second-order process evaluation data consisting of knowledge on the implementation strategy and factors affecting implementation is evaluated to improve further implementation [10].

First-order process evaluation

To evaluate *sample quality* a description was provided of (1) the recruitment and randomization of the YOD SCUs, and (2) the recruitment and informed consent procedure of the NH residents. Also, intervention reach was described by (3) a description of the proportion of residents participating in the study in relation to the number of residents eligible for inclusion, and (4) the proportion of staff involved in the use of the care program.

Intervention quality was determined by (1) the satisfaction with and relevance of the care program, (2) the feasibility of the care program, and (3) fidelity of the intervention. The satisfaction with and relevance of the care program were investigated at the end of the study with a questionnaire, which was distributed among vocational nurses, physicians, and psychologists. Participants were asked if they would recommend the care program to other colleagues (answer categories: yes, no, unknown). Additionally, for each step of the care program (Figure 1) they were asked if they perceived it as relevant steps in the management of NPS (answer categories: yes, no, unknown).

In order to investigate feasibility, participants were asked if they were able to perform the care program in the current available time on a questionnaire (answer categories: yes, no). Fidelity of the intervention was evaluated by establishing the proportion of the multidisciplinary team participating in an educational program (which was part of the implementation strategy). In addition, the extent to which the care program was performed for each NH was logged on the server of the web-based environment providing data on the number of identified residents with NPS and data on how often each step of the care program was completed.

Second-order process evaluation

A detailed description of the implementation strategy used alongside the intervention was provided. Furthermore, barriers and facilitators for the implementation of the intervention were inventorized through open ended questions on a questionnaire.

Data collection procedure

Quantitative data were analyzed with the Statistical Package for the Social Sciences (SPSS) version 22 by calculating descriptive data (frequencies, percentages, and standard deviations). In order to analyze the qualitative data, a deductive content analysis was performed [37]. The first author (B.A) developed a structured analysis matrix based on the implementation knowledge of the original care program developed in the 'Grip on challenging behavior' study [18, 22]. This study identified three themes of implementation knowledge: organizational aspects, culture of

the organization, and aspects of the intervention. Two authors (J.D. and B.A.) coded the data for correspondence with the themes separately. Disagreements were solved by discussion.

Results

First-order process evaluation

Recruitment and randomization of young-onset dementia special care units
YOD special care units (SCUs) were recruited through NHs that are affiliated with the Dutch YOD Knowledge Center (DKC). Twenty-five NHs were approached of which 15 decided to participate. Two YOD SCUs were excluded because they were considered to small (less than 12 residents). Reasons for refusing to participate were planned reorganizations and participation in other research projects. The thirteen SCUs which participated varied in size at time of inclusion (Mean = 25.9 residents, SD = 11.9). The SCUs were located in different geographical regions of the Netherlands of which five in the densely populated western part of the Netherlands.

Recruitment and informed consent procedure of the NH residents
The inclusion and exclusion criteria [9] were provided to staff of the participating YOD SCUs for the initial selection of residents eligible for the study. The NH staff provided the legal representatives of the residents who probably met inclusion criteria with informed consent (IC) forms and folders with information about the study. The SCU implemented the intervention on an unit level. Therefore, all legal representatives were informed that also residents without IC would be exposed to the intervention. To respect privacy, no data on demographic characteristics and the presence of NPS was collected by researchers from residents of which IC was not provided. During the study, deceased residents could be replaced by newly admitted residents.

Residents' reach
Before the first assessment, IC was provided for 213 (87.7%) residents. In eleven SCUs IC was provided for more than 87.0% of the residents and in two SCUs approximately 60.0% of the legal representatives did provide IC (Figure 2). At each of the four assessments, approximately 15 percent of the participating residents had moved to another unit or had deceased. Of the newly admitted residents, only few legal representatives did not provide IC. Although IC was often provided for newly admitted residents, there was a small decline in the number of residents participating in the study (Figure 2). This decline was due to a decrease in size of the SCUs. Two SCUs closed beds due to organizational changes.

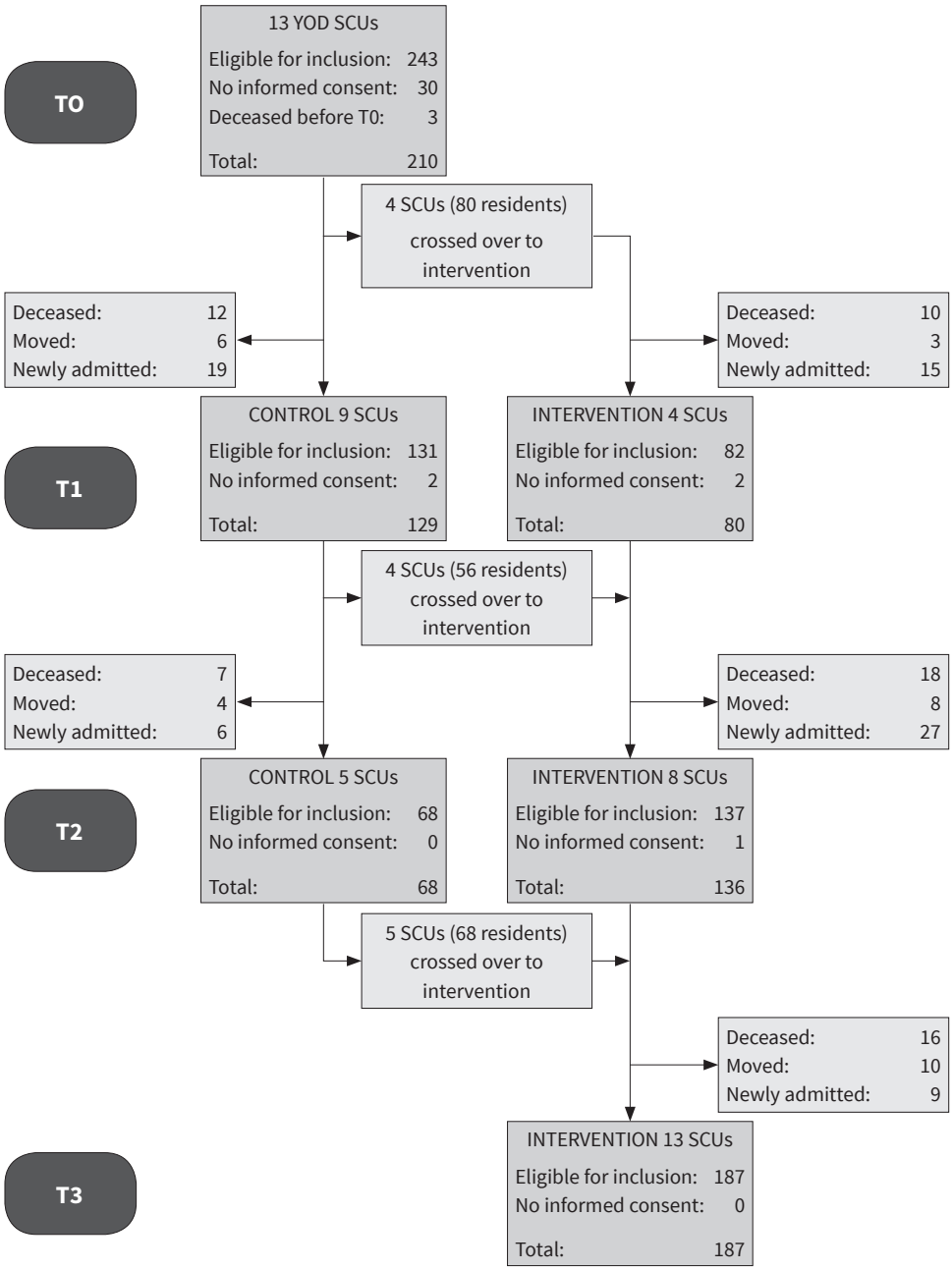

Figure 2. Results of recruitment of the residents of the Beyond-II study.
YOD SCU = Young onset dementia special care unit
There were four, half yearly, assessments: T0, T1, T2, T3.

Nursing home staff reach

In total, 323 nurses, 16 psychologists, 16 physicians, and 9 team leaders were involved in the use of the care program at time of the first assessment. Of these, 23.8% (N = 77) of the nursing staff, 25.0% (N = 4) of the psychologists, 25.0% (N = 4) of the physicians, and 44.4% (N=4) of the team leaders were not working on the SCU anymore at the last assessment. Main reasons were organizational changes, transfer to another unit or other health care organization, retirement, or maternity leave. For all physicians and psychologists who left during implementation, new clinicians were employed. They received information and instruction about the care program from colleagues or from one of the researchers. Four team leaders left due to organizational changes and were not replaced.

The satisfaction with and relevance of the care program

At time of the last assessment, eighty-two NH staff members (74.6%) responded on a web-based questionnaire. Fifty-eight percent (N = 35) of the respondents was satisfied with the overall content of the care program, and 55.0% (N = 33) would recommend the care program to other colleagues. The step analysis by the nursing staff was perceived as the most relevant in the management of NPS (perceived as relevant by 43.9%, N = 29) (Table 1.). After the analysis by the nursing staff, the step evaluation was perceived as most relevant in the treatment of NPS (perceived as relevant by 42.1%, N = 8). The critical appraisal of the appropriateness of PDU was most often perceived as irrelevant (83.3%, N = 5).

Feasibility of the care program

With regard to the feasibility of the care program, most respondents (61.9%, N = 39) stated that it was not feasible to use the care program in the time available to them in day to day practice. Especially the steps ‘analysis by the nursing staff’ and the ‘detection of unmet needs’ were rated as too time consuming.

Table 1. Perceived relevance of each step of the care program by nursing home staff members.

	Relevant	Irrelevant	Not able to rate
Detection	27.50 % (N = 19)	49.30% (N = 34)	23.2% (N = 16)
Analysis nurses	43.90% (N = 29)	30.30% (N = 20)	25.80% (N = 17)
Needs assessment [a]	34.50% (N = 20)	19.00% (N = 11)	46.60% (N = 27)
Involving family in needs assessment	29.50% (N = 13)	13.60% (N = 6)	56.80% (N = 15)
Analysis clinician [b]	37.50% (N = 9)	37.50% (N = 9)	25.00% (N = 6)
Treatment [b]	31.80% (N = 7)	36.40% (N = 8)	31.80 (N = 7)
Evaluation [b]	42.10% (N = 8)	26.30% (N = 5)	31.60% (N = 6)
PDU assessment [c]	16.70% (N = 1)	83.30% (N = 5)	-

[a] Part of analysis nurses;

[b] Only rated by psychologists and physicians;

[c] Only rated by physicians.

22.7% (N=25) of the questionnaires were incomplete. Questions that were available were also included in the analysis.

Fidelity of the intervention

Of the nursing staff, 48.0% (N = 155, SD = 24.3) participated in the educational program (part of the implementation strategy). In three SCUs 76.0-95.0% participated, in six 32.0-54.0% participated, and in four SCUs 17.0-26.0% participated. With regard to the clinicians, 50.0% (N = 8) of the psychologists and 43.8% (N = 7) of the physicians participated in the educational program. Of the nine SCUs that employed a team leader, all but one team leader (88.9%, N = 8) participated in both training sessions. The main reasons for both the nursing staff and the clinicians not participating were being on leave or ill.Server logs of the care program showed that the care program was used for 368 residents (range per SCU = 6-66 residents). Although we only collected data from residents who met inclusion criteria and for whom IC was provided, the anonymous server logs also contain residents not participating in the study. This might result in an overestimation of fidelity. Furthermore, after detection and analysis, the NH staff may conclude there are no signs of NPS (Figure 1). Therefore, the number of times the steps 'treatment' and 'evaluation' are completed will be lower compared to the other steps. The step of the detection of NPS was performed most often (completed 415 times). The step of the construction of a treatment plan was used the least (completed 41 times), followed by the PDU assessment (completed 45 times) (Table 2). Fidelity differed between SCU's. One SCU did only perform the step detection twice. The assessment of PDU was not (or only once) used by nine

SCU's. Six SCU's did not (or only once) use the later steps of the care program: treatment and evaluation.

Table 2. The extent to which each step of the care program was performed.

	Unit size[a] (residents)	Group[b]	Residents in care program[c]	PDU assess-ment[d]	Detection	Analysis nurses (after screening tool)[e]	Analysis clinician	Treatment [f]	Evaluation [f]
YOD SCU number									
1	36	1	49	1	95	56 (42)	43	6	6
2	48	1	66	1	129	106 (85)	99	11	17
3	32	1	32	0	42	29 (24)	14	2	2
4	18	1	22	11	33	36 (26)	22	1	1
5	14	2	16	0	11	7 (3)	5	0	0
6	14	2	13	12	16	9 (4)	8	2	2
7	18	2	22	0	2	14 (2)	21	10	14
8	45	2	37	0	9	10 (7)	10	0	0
9	22	3	39	12	16	18 (10)	18	5	3
10	21	3	6	0	6	5 (5)	7	0	0
11	20	3	20	8	19	13 (11)	9	1	1
12	35	3	39	0	28	18 (15)	11	3	7
13	14	3	7	0	9	8 (7)	11	0	0

[a] At time of inclusion (T0).

[b] Period of working with care program Group 1: 18 months, Group 2: 12 months, Group 3: 6 months.

[c] Including residents who moved, deceased, and newly admitted residents during implementation, and residents residing on the care unit who did not participate in the study. Therefore, for a SCU the unit size can be smaller than the number of residents in the care program.

[d] Times each step of the care program was completed.

[e] Times that the analysis was followed after the screening tool for the detection of NPS revealed symptoms of NPS. The remaining times followed after the detection of NPS in daily observations (without the use of the screening tool).

[f] Step is only completed if step analysis nurses reveals NPS and clinician perceives treatment as necessary. Therefore, these steps will be less often completed compared to the other step.

YOD SCU = young onset dementia special care unit.

Second-order process evaluation

Implementation strategy

A multi-component implementation strategy was used to increase acceptability (the perception that the care program is satisfactory) and adoption (the intention to use) of the NH staff and increase feasibility, fidelity, and sustainability (the extent to which the care program will be maintained) of the intervention [12, 21]. The strategy was based on perceived barriers in implementation of the original care program in LOD [18].

In order to increase acceptability and adoption, at the start of the implementation the NH staff received an educational program that consisted of two training sessions (of 2.5 hours and 1.5 hours respectively). In the educational program, the causes and mechanisms of NPS were explained and the need for a specific intervention in YOD was discussed. In addition, instruction in the use of the care program was provided. This educational program was given by one of the authors (J.D. or B. A.). In order to increase fidelity and sustainability, six months after implementation, all NH staff received an additional training (of 1.5 hours). In this training session, facilitators and barriers for implementation of the care program in the own organization were discussed and the NH staff was stimulated to think about how to address these barriers and therewith facilitate further implementation.

In order to increase acceptability, fidelity, and sustainability a champion supporting the implementation of the care program was appointed in all participating YOD SCUs. The NH staff working on the YOD SCUs decided on who would become champion using the following selection criteria: has to be a user of the care program or closely involved (e.g. team leader), has to have leadership in the multidisciplinary team (e.g. vocational nurse, physician, psychologist, or team leader), has to be easy to approach, has to be supporting of the care program, and has to be capable of motivating the team. Together with this champion, possible barriers and facilitators for successful implementation were explored using a questionnaire before and every six months during the implementation of the intervention. If possible, the barriers were addressed and facilitators were used to further enhance implementation in that particular SCU.

In the original care program, providing the care program on paper forms was perceived as a barrier for implementation since this did not attune with the current working methods and electronic health records [18]. Therefore, in order to increase feasibility, the current care program was offered in a web-based format.

Factors affecting implementation

Data on barriers and facilitators for implementation were organized into the three major themes identified in previous implementation research [18, 22]: organizational aspects, culture of the organization, and aspects of the intervention (Table 3).

Organizational aspects

Barriers from an organizational perspective were high rates of temporary staff or low educated staff and organisational changes (e.g. renovations or transitions towards self-directed teams). In addition, high rates of staff turnover was perceived as a barrier, as new staff members were not always well informed about the care program and needed time to get acquainted with the use.

An organizational facilitator was limited involvement in new research projects during the implementation of the care program that could interfere with carrying out the care program. In addition, regular multidisciplinary meetings were perceived as a facilitator. Several SCUs, in which the disciplines did not meet each other regularly, started with multidisciplinary meetings (at least once every two weeks) before implementation of the care program.

- *''Being made aware that involvement in new research projects could interfere with implementation, made it easier to reject requests for participation of the care unit in other important projects''.[P7]*

Culture of the organization

A barrier related to the culture of the organisation was lack of involvement of the multidisciplinary team in the educational program. Involvement in the educational program increased commitment and motivation in the use of the care program. However, not all NH staff participated.

A cultural facilitator was the openness to changing working routines. The NH staff often mentioned that they found it necessary that a care program for the management of NPS would be implemented on their care unit and were confident that the care program would diminish NPS, which made them more eager to invest time in implementation.
In addition, the support of the champion and support of the management were often mentioned as facilitators for implementation.

Table 3. Facilitators and barriers during the implementation.

Themes	Categories	Barrier	Facilitator
Organizational aspects			
	Multidisciplinary collaboration		Regular multidisciplinary meetings facilitated collaboration and regular contact in which the forms were discussed.
	Staff shortage	High rates of temporary staff or low educated staff increased the workload and hindered implementation.	
	Staff turnover	New staff members were not always well informed and did therefore not work according to the intervention. Also, when new staff members did receive sufficient instruction in the use, it took time to really get acquainted with the use.	
	Organizational changes	Changes like renovation of the care unit or transition towards self-directed teams interfered with implementation of the care program.	
	Involvement in other projects		Limited involvement in new (research) projects which could interfere with carrying out the care program.

Culture of the care unit		
	Openness to the change in working routines and procedures	NH staff that expected the care program to be beneficial and agreed with participation in the study were more eager to invest time.
	Support of the ambassador	An ambassador which motivated involved disciplines facilitated implementation.
	Support of the management	Some care units received extra budget from the management to facilitate successful implementation.
	Involvement in educational program	Involvement of the whole multidisciplinary team (nursing staff, psychologist, elderly care physician) in the educational program increased commitment and motivation for the use of the care program. However, not all NH staff participated.
Aspects of the intervention		
	Overlap with current working method	Overlap between steps of the care program and the NHs usual working methods in the management of NPS.

- *'Implementation is time consuming and sometimes frustrating. To be honest, we are still not there yet. However, I believe our residents will benefit from this intervention and therefore we will continue with implementation''. [A12]*

Aspects of the intervention

Respondents mentionded overlap with curent working methods, especially with tools already available in the electronic health record. Because it was mandatory to report information on the management of NPS in the electronic health record, the NH staff was more inclined to continue to work according to their old working routine. No facilitators were revealed within this theme.

- *''We did not let go our own working methods during implementation. In addition to the forms of the digital care program, it was mandatory to still use our own forms in the electronic health record. In my experience this doubled the work''. [Z5]*

Discussion

First-order proces data on validity showed that the participating SCUs varied in size and location. The informed consent rate of the residents was 87.7%. Most NH staff members were satisfied with the overall content of the care program. However, parts of the intervention were perceived as less relevant for the own organization. The feasibility of the intervention was considered low. The fidelity differed between steps of the care program and SCUs. Second order process data on implementation showed that staff turnover and shortage, organizational changes, lack of involvement in educational program, and overlap with current working methods were barriers for implementation. Facilitators for implementation were multidisciplinary collaboration, limited involvement in other projects, openness to change in working procedures, and support of the ambassador and management.

First-order process evaluation

The variety in size of the SCUs and the location of the SCUs in different geographical regions of the Netherlands, the high proportion of residents with IC, and the sufficient sample size allow for effect analyses and generalization of the study effects.

The differences in perceived relevance and low feasibility of steps of the care program can negatively influence the applicability of the intervention and therewith hinder external validity. Adaptations to increase relevance and feasibility of some steps of the care program should be considered. The analysis by the nursing staff was most often rated as too time consuming and the need assessment in this analysis was not perceived relevant for all residents (i.e. in advanced dementia or for residents who had been residing on the SCU for a long period). In order to increase the relevance and feasibility, the need assessment could be changed into an optional step in the care program reserved for newly admitted residents or residents which needs are still unclear according to the vocational nurse. However, one should be aware that an extensive (and therewith possibly time consuming) analysis of the behavior is a precondition to indentify the underlying cause. Therefore, special attention needs to be directed to strategies to further increase adoption of the care program by the NH staff.

Fidelity of the intervention was not optimal. The low participation rates in the educational program in some SCUs and the differences in degree of implementation between steps of the care program, will likely reduce the effectiveness of the intervention and therewith decrease internal validity. To investigate possible differences in effects due to low treatment fidelity in some SCUs, subgroup analysis including participation rate and care program performance should be part of the effect analyses.

Second-order process evaluation

Despite the use of an implementation strategy which was successful in addressing some of the barriers already known from previous research, the implementation of the care program was not optimal. Some barriers known in advance, like staff turnover, staff shortage, and organizational changes, are part of daily practice and could not be resolved [18-22].

In addition, steps of the program did not add to the working methods from the perspective of the NH staff. For instance, in some SCUs a screening tool for NPS was already available in the electronic health record. In order to create commitment to change the old working routine, the staff needs to believe in the benefits of the intervention for the own organization [27]. Therefore, we believe that perceived irrelevance of some steps of the care program hindered implementation. In future implementation, more attention needs to be paid to the appropriateness (the compatibility of the intervention for the given setting) for the own organisation [12]. Integration of the care program in the electronic health record could prevent overlap with current working methods. In addition, relevance of the intervention might increase if it is tailored to the specific working method of a specific SCU, rather than completely standardized [38].

In order to increase fidelity by improving the participation rate of the NH staff in future implementation studies, changing the structure of the educational program could be considered. NH staff usually works according to a schedule. Enabling the NH staff to follow training in the intervention at different times and/or several days, will likely create the opportunity for more NH staff members to participate [39]. This would also allow staff members who are on leave or ill, the main reasons for not participating in our educational program, to participate.

Furthermore, although assigning champions indeed facilitated implementation, the dependency on one champion might make implementation vulnerable. Should the designated champion be less competent or depart, this would negatively impact sustainability. For future implementation, it could be helpful to share the responsibilities of the champion among several staff members.

At last, in future implementation studies the readiness for change needs to be taken into account in order to increase adoption [40]. For example, in our study, the high prevalence rates of PDU in YOD and the high rates of inappropriate psychotropic drugs prescription found in dementia stresses the need for a tool for the evaluation of appropriateness of psychotropic drug prescription [1, 2, 41]. However, almost all physicians in our study perceived the tool as irrelevant, suggesting that they did not perceive changes were needed: hindering adoption. In order to increase the readiness to

change, more education specifically for the elderly care physicians about the importance of the tool before implementation could have been helpful [42]. Another solution might be to integrate the tool in the step 'detection', instead of using it as a separate step in the care program which could be used at the users' own discretion. Consequently, the physicians would need to use the tool systematically every six months for all residents. By using the tool, they might perceive its benefit and therewith become more accepting. However, we should be aware that forcing the use of the tool could also create resistance and therewith hinder implementation [42].

Conclusions

First-order proces data revealed that the SCUs varieted in size and location, the sample sizes were large enough to establish clinical relevant effects, and most respondents were satisfied with the overall content of the intervention. Therefore, sample and intervention quality allow for effect analyses.

With regard to the second-order process data, the implementation strategy was successful in addressing some of the barriers already known from previous research. However, it was impossible to control for all contextual influences. Still, we expect that creating awareness of these inevitable barriers before implementation, will somewhat have diminished their negative influence on the implementation process. Adaptations to specific steps of the care program should be considered to increase feasibility and relevance. We expect that integration of the care program in the electronic health records will further improve implementation. Also, tailoring the care program to the specific working method of each SCU should be considered. For future implementation studies, it is important to include strategies that take into account the readiness to change of the NH staff and increase commitment.

References

1. Mulders AJMJ, Fick IWF, Bor H, et al.: Prevalence and correlates of neuropsychiatric symptoms in nursing home patients with young-onset dementia: The BEYOnD Study. Journal of the American Medical Directors Association 2016;17(6):495-500.
2. Mulders AJMJ, Zuidema SU, Verhey FR, Koopmans RTCM: Characteristics of institutionalized young onset dementia patients – the BEYOnD study. International Psychogeriatrics 2014;12:1973–81.
3. Wetzels R, Zuidema S, de Jonghe J, et al.: Determinants of quality of life in nursing home residents with dementia. Dement Geriatr Cogn Disord 2010;29(3):189-97.
4. Murman DL, Chen Q, Powell MC, et al.: The incremental direct costs associated with behavioral symptoms in AD. Neurology 2002;59:1721–9.
5. Zwijsen SA, Kabboord A, Eefsting JA, et al.: Nurses in distress? An explorative study into the relation between distress and individual neuropsychiatric symptoms of people with dementia in nursing homes. International Journal of Geriatric Psychiatry 2014; 29(4):384-91.
6. Ballard CG, Margallo-Lana ML: The Relationship Between Antipsychotic Treatment and Quality of Life for Patients With Dementia Living in Residential and Nursing Home Care Facilities. J Clin Psychiatry 2004;65:23-8.
7. Gonzalez-Salvador T, Lyketsos CG, Baker A, et al.: Quality of life in dementiapatients in long-term care. Int J Geriatr Psychiatry 2000;15:181-9.
8. Appelhof B, Bakker C, van Duinen-van den IJssel JCL, et al.: The Determinants of Quality of Life of Nursing Home Residents with Young-Onset Dementia and the Differences between Dementia Subtypes. Dement Geriatr Cogn Disord 2017;43:320 329.
9. van Duinen-van den IJssel JCL, Appelhof B, Zwijsen SA, et al.: Behavior and Evolution of Young-ONset Dementia part 2 (BEYOND-II) study: an intervention study aimed at the improvement of the management of challenging behavior in institutionalized people with young-onset dementia International Psychogeriatrics 2017;Epub ahead of print.
10. Leontjevas R, Gerritsen DL, Koopmans RTCM, et al.: Process Evaluation to Explore Internal and External Validity of the “Act in Case of Depression” Care Program inNursing Homes. Journal of the American Medical Directors Association 2012;13(5):488.e1-.e8.
11. Eldridge S, Ashby D, Bennet C, et al.: Internal and external validity of cluster randomised trials: systematic review of recent trials. BMJ 2008;336(7649):876-80.

12. Proctor E, Silmere H, Hovmand P, et al.: Outcomes for implementation research: conceptual distinctions, measurement challenges, and research agenda. Administration and Policy in Mental Health and Mental Health Services Research 2011;38(2):65-76.
13. Peters DH, Taghreed A, Agyepong A, et al.: Implementation research: what it is and how to do it. BMJ 2013;347:1-7.
14. Vernooij-Dassen M, Moniz-Cook E: Raising the standard of applied dementia care research: addressing the implementation error. Aging and Mental Health 2014;18(7):809-14.
15. Oakley A, Strange V, Bonell C, et al.: Process evaluation in randomised controlled trials of complex interventions. BMJ 2006;332:413–6.
16. Rychetnik LL, Frommer M, Hawe P, Shiell A: Criteria for evaluating evidence on public health interventions. Journal of Epidemiology and Community Health 2017;56(2):119-27.
17. Moore G, Audrey S, Barker M, et al.: Process evaluation of complex interventions: Medical Research Council guidance. BMJ 2015;350:1-7.
18. Zwijsen SA, Smalbrugge M, Eefsting JA, et al.: Grip on challenging behavior: process evaluation of the implementation of a care program. Trialsjournals 2014;15:2-11.
19. Mentes JC, Tripp-Reimer T: Barriers and facilitators in nursing home intervention research. Western Journal of Nursing Research 2002;24(8):918-36.
20. van de Ven G, Draskovic I, Adang EMM, et al.: Effects of dementia-care mapping on residents and staff of care homes: a pragmatic cluster-randomised controlled trial. PLoS One 2013;8(7):1-7.
21. Proctor EK, Powell BJ, McMillen JC: Implementation strategies: recommendations for specifying and reporting. Implementation Science 2013;8:139.
22. Zwijsen SA, Gerritsen DL, Eefsting JA, et al.: The development of the Grip on Challenging Behaviour dementia care programme. International journal of palliative nursing 2014;20(1):15-21.
23. Zwijsen SA, Smalbrugge M, Zuidema SU, et al.: Grip on challenging behaviour: a multidisciplinary care programme for managing behavioural problems in nursing home residents with dementia. Study protocol. BMC Health Services Research 2011;11(41):1-6.
24. Zwijsen SA, Gerritsen DL, Eefsting JA, et al.: Coming to grips with challenging behaviour: a cluster randomised controlled trial on the effects of a new care programme for challenging behaviour on burnout, job satisfaction and job demands

of care staff on dementia special care units. International journal of nursing studies 2015;52(1):68-74.
25. Zwijsen SA, Smalbrugge M, Eefsting JA, et al.: Coming to grips with challenging behavior: a cluster randomized controlled trial on the effects of a multidisciplinary care program for challenging behavior in dementia. Journal of the American Medical Directors Association 2014;15(7):1-531.
26. Koopmans RCTM, Pellegrom M, van der Geer ER: The Dutch Move Beyond the Concept of Nursing Home Physician Specialists. Journal of the American Medical Directors Association 2017;Epub ahead of print.
27. Ribbe MW, Ljunggren G, Steel K, et al.: Nursing homes in 10 nations: a comparison between countries and settings. Age and Ageing 1997;26:3-12.
28. Kaufer DI, Cummings JL, Ketchel P, et al.: Validation of the NPI-Q, a brief clinical form of the Neuropsychiatric Inventory. J Neuropsychiatry Clin Neurosci 2000;12:233-9.
29. Orrell M, Hancock G: CANE: Camberwell Assessment of Need for the Elderly, Gaskell, 2004.
30. Reynolds TT, Thornicroft G, Abas M, et al.: Camberwell Assessment of Need for the Elderly (CANE). Development, validity and reliability. The British Journal of Psychiatry 2000;176:444-452.
31. Verpleegkundigen & Verzorgenden Nederland (V&VN): Richtlijn omgaan met gedragsproblemen bij patiënten met dementie, Nijmegen, V&VN, 2005.
32. Nederlands Instituut van Psychologen (NIP): Handreiking Psychologische hulpverlening bij gedragsproblemen bij dementie, Amsterdam, NIP, SPO, 2013.
33. Verenso: Richtlijn Probleemgedrag bij mensen met dementie, Verenso, 2018.
34. van der Spek K, Gerritsen DL, Smalbrugge M, et al.: PROPER I: frequency and appropriateness of psychotropic drugs use in nursing home patients and its associations: a study protocol. BMC Psychiatry 2013;13:1-7.
35. van der Spek K, Gerritsen DL, Smalbrugge M, et al.: A reliable and valid index was developed to measure appropriate psychotropic drug use in dementia. Journal of Clinical Epidemiology 2015;68(8):903-12.
36. Linnan N, Steckler A: Process evaluation for public health interventions and research: An overview, San Francisco, Jossey Bass, 2002.
37. Elo S, Kyngas H: The qualitative content analysis process. Journal of Advanced Nursing 2008;62(1):107-115.
38. Craig P, Dieppe P, Nazareth I, Petticrew M: Developing and evaluating complex interventions: the new Medical Research Council guidance. BMJ 2008;337:1-6.

39. Boersma P, van Weert JCM, Lakerveld J, Droes RM: The art of successful implementation of psychosocial interventions in residential dementia care: a systematic review of the literature based on the RE-AIM framework. International Psychogeriatrics 2015;27(1):19-35.

40. Choi M: Employees'attitudes toward organizational change: a literature review. Human Resource Management 2011;50:479-500.

41. van der Spek K, Gerritsen DL, Smalbrugge M, et al.: Only 10% of the psychotropic drug use for neuropsychiatric symptoms in patients with dementia is fully appropriate. The PROPER I-study. International Psychogeriatrics 2016;28(10):1589-95.

42. Kotter JP, Schlesinger LA: Choosing Strategies for Change. Harvard Business Review 1979;57:106-14.


Family
I'm glad I
I love you
I wish I could remember
Pain
New challe
help
happiness
love
love life
how
Take care of the children
I forgot
I don't know
Golden years
enjoy
Good life
Work
learning
why
angry
I have
Friends
to grow
away from home
the beginning

Chapter 6

BEYOND-II EFFECT STUDY

Effects of a multidisciplinary intervention on the presence of neuropsychiatric symptoms and psychotropic drug use in nursing home residents with young-onset dementia: Behavior and Evolution of Young ONset Dementia part 2 (BEYOND-II) study

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Abstract

Objectives: An intervention that has shown effectiveness in the management of neuropsychiatric symptoms (NPS) in institutionalized people with dementia was specifically tailored for the use in institutionalized people with young-onset dementia (YOD). The effect of the intervention on the presence of NPS, particularly agitation and aggression, and psychotropic drug use (PDU) in YOD was evaluated.
Design/ Setting: A randomized controlled trial was conducted using a stepped wedge design. Thirteen YOD special care units were randomly assigned to three groups, which received the intervention at different time points. Four assessments took place every six months during a period of eighteen months.
Participants: Two hundred and seventy-four people with YOD residing on YOD special care units participated, of whom 131 in all assessments.
Intervention: The intervention consisted of an educational program combined with a care program, which structured the multidisciplinary process of managing NPS. The care program included the following five steps: the evaluation of psychotropic drug prescription, detection, analysis, treatment and evaluation of treatment of NPS.
Measurements: The Cohen-Mansfield Agitation Inventory and the Neuropsychiatric Inventory, nursing home version were used to assess NPS. Data on PDU was retrieved from residents' medical files. Multilevel models were used to evaluate the effect of the intervention, which accounted for clustering of measurements within clients, within units.
Results: No significant differences on agitation and aggression, other NPS, and PDU after crossing over to the intervention condition were found.
Conclusions: The intervention for the management of NPS in nursing home residents with YOD was not more effective in reducing agitation and aggression, other NPS, or PDU compared to care as usual.

Introduction

Young-onset dementia (YOD) is defined as dementia with symptom onset before the age of 65. In nursing home (NH) residents with YOD, neuropsychiatric symptoms (NPS) are common [1]. NPS encompass various symptoms such as depression, anxiety, apathy, aggression, agitation, disinhibition, delusions, and hallucinations. Mulders et al. found in the Behavior and Evolution of Young ONset Dementia, part 1 (Beyond-I) study that 90% of NH residents with YOD showed one or more NPS [1][11]. These high rates are troublesome given the serious negative health outcomes associated with NPS in dementia, such as loss of quality of life of the NH resident, high workload for NH staff, and increased costs of care [2-5]. Agitated behaviors are highly prevalent in YOD. Especially agitated behaviors are strongly related to distress of professional caregivers and to reduced quality of life in both NH residents with late-onset dementia (LOD) and YOD [3-7]. Psychotropic drug use (PDU) is common in the management of NPS in NH residents with LOD and YOD [8, 9]. PDU is associated with poor health outcomes, such as stroke, increased mortality, and reduced quality of life [3, 10, 11]. Therefore, Dutch guidelines for the management of NPS in dementia recommend that pharmacological interventions should be temporary and only be used if psychosocial interventions have little or no effect [12-14]. However, still between 76.9 - 87.6 % of the NH residents with YOD use one or more psychotropic drug(s) [4, 8]. Those rates seem higher compared to PDU in NH residents with LOD [8].

The high prevalence rates of NPS and PDU in YOD stresses the need for effective nonpharmacological interventions especially in the management of NPS in YOD.
To successfully manage NPS, many models emphasize that the underlying causes of NPS need to be identified and treated [15]. One of these models is the unmet-needs framework, in which NPS are perceived as behaviors through which the person with dementia might indirectly communicate an underlying need [15]. Needs can be medical (e.g. physical illness, pain, mobility), psychosocial (e.g. life habits, premorbid personality), or environmental (e.g. under/over stimulation, behavior of NH staff/ other residents) [16, 17]. With knowledge of the underlying causes of NPS, an intervention can be individualized to the specific needs of the residents, instead of suppressing the behavior with the use of psychotropic drugs, concealing behavior through which the person with dementia might indirectly communicate an underlying need [16, 18, 19]. People with YOD have specific age-related care needs regarding daytime activities, social interaction, intimate relationships, and information [20]. These care needs are often unmet [20]. In community-dwelling people with YOD these unmet care needs are strongly related to the presence of NPS [20]. It is

likely that the same relation between unmet care needs and NPS applies to NH residents with YOD. Therefore, in order to decrease the high rates of NPS in NH residents with YOD, these specific needs should be addressed.

In the Netherlands, a multidisciplinary team including nursing staff, elderly care physicians and psychologists is involved in the management of NPS in NHs [21, 22]. In the current study, an intervention which provides guidance for these disciplines to properly work together to identify and to treat the underlying causes of NPS in YOD specifically was developed. The intervention was based on The "Grip on challenging behavior" care program that has shown effectiveness in the management of NPS in LOD [23-26]. In order to address the high levels of unmet care needs and high prevalence rates of PDU in YOD, a tool for the detection of unmet needs [27] and a tool for the evaluation of appropriateness of psychotropic drug prescription [28]) were added to the original intervention [29].

The aims of the study are to (1) evaluate the effect of the intervention on the prevalence of NPS, particularly agitation and aggression, compared to care as usual, and (2) evaluate the effect of the intervention on PDU.

Methods

This cluster randomized controlled trial (RCT) is part of the Behavior and Evolution of Young-ONset Dementia, part 2 (Beyond-II) study. The full study protocol has been published elsewhere [29]. In a previous study, process data was assessed in order to be able to interpret the outcomes of this RCT [30]. In general, the process data showed sufficient internal (the extent to which effects are a result of the intervention) and external (the generalizability of the effects of the intervention) validity allowing for further effect analyses [30, 31].

Setting and subjects

Recruitment procedures and reach of the YOD special care units (SCUs) and NH residents are described in more detail elsewhere [30]. In short, in this study thirteen YOD SCUs participated, which are care units delivering specialized treatment and support for people with YOD. The YOD-SCUs were recruited through NHs that are affiliated with the Dutch YOD Knowledge Center (DKC). Residents with a dementia diagnosis with a symptom onset before the age of 65 who resided on the YOD SCU for at least one month were eligible for inclusion in the study. The exclusion criteria were lack of informed consent provided by the

legal representative, dementia caused by human immunodeficiency virus (HIV), traumatic brain injury, Down's syndrome, Korsakov syndrome or Huntington's disease. Diagnoses of dementia subtype were made before inclusion, according to internationally accepted criteria for diagnosing dementia subtypes and were retrieved from medical files [32-37]. Newly admitted residents were recruited until the end of the study, replacing deceased residents and residents who moved to another care unit during the study.

Intervention

The development of the intervention 'Grip on NPS in institutionalized people with YOD' is described in detail elsewhere [29]. The intervention consisted of an educational program and a web-based care program. The educational program involved two training sessions (of 2.5 and 1.5 hours respectively) in which causes and mechanisms of NPS were discussed with the NH staff and the use of the care program was explained. After receiving the educational program, the care program on the management of NPS was implemented (figure 1). This care program provided a structural multidisciplinary approach on the management of NPS, consisting of five steps. The first and separate step was a tool for the evaluation of appropriateness of psychotropic drug prescription by the elderly care physician. The tool was adapted and extended based on the Appropriateness of Psychotropic Drug Prescription In Dementia (APID)-instrument [28, 38, 39]. The tool was performed for all residents (with or without NPS) in the first two months after the SCU was enrolled in the intervention condition. After the initial screening, the tool was used at the physician's own discretion. The other four consecutive steps of the care program had a circular structure (figure 1). Detection of NPS occurred through usual observations of the multidisciplinary team or with the systematic use of a screening tool every six months by a vocational nurse (or by a nurse who had regular contact with the resident in the past month). When NPS were detected, a structured analysis of possible causes of the NPS observed was conducted by the (vocational) nurse. This analysis included a tool for the detection of unmet needs possibly underling the NPS. The tool was adapted and extended based on the Dutch version of the Camberwell Assessment of Need for the Elderly (CANE) [27]. When necessary, the elderly care physician and/or the psychologist continued the analysis. After this analysis, treatment options were discussed within the multidisciplinary team and a treatment plan was established by the elderly care physician and/or the psychologist. The treatment outcomes were evaluated by the multidisciplinary team and if unsatisfactory, other treatments were considered or the analysis was performed again. All tools of the care program were fully digitalized and contained automatic reminders.

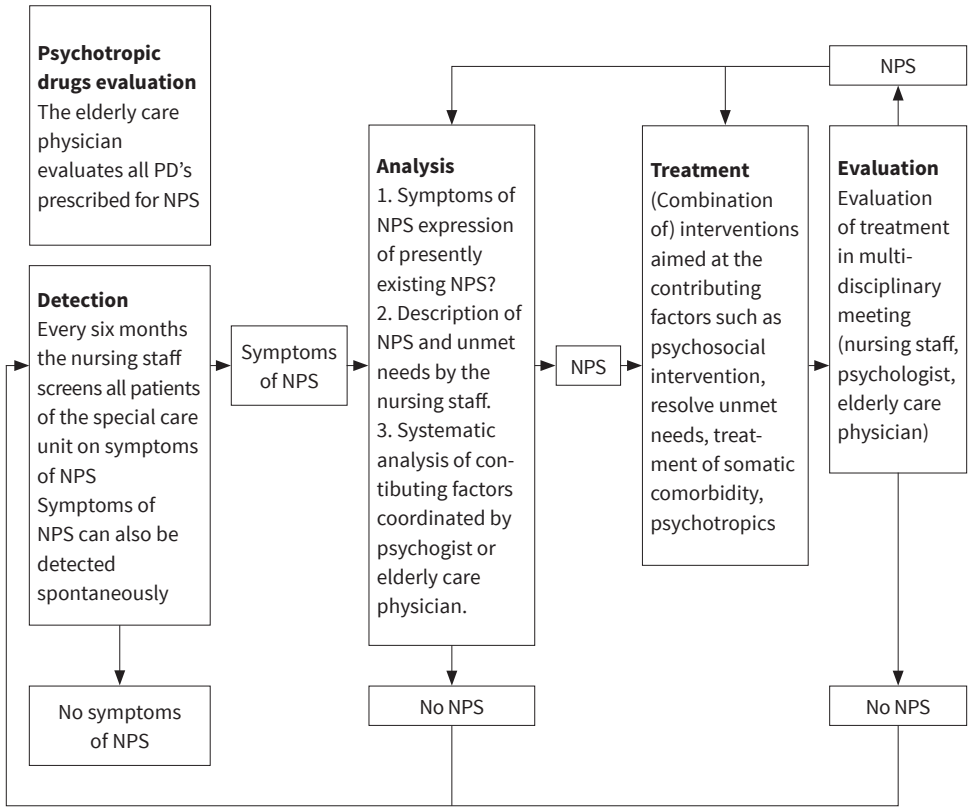

Figure 1. The five steps of the care program 'Grip on NPS in institutionalized people with YOD [29].

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NPS = Neuropsychiatric Symptoms; PD's = Psychotropic Drugs.

6

Design

To evaluate the effect of the intervention, a stepped wedge design was used (Table 1). This design allows clusters (in this study groups of YOD SCUs) to crossover from the control to the intervention condition over time, assuring that all YOD SCUs received the intervention [40]. The thirteen YOD SCUs were randomly assigned to three groups. Every six months a new group entered the intervention condition. The control condition consisted of care as usual without the educational program and use of the care program. Four assessments took place every six months during a period of eighteen months (September 2015 - April 2017): before implementation (T0), during implementation (T1 and T2) and at the end of implementation (T3).

Table 1. Stepped wedge design [29].

	Group 1	Group 2	Group 3
T0	0	0	0
T1	1	0	0
T2	1	1	0
T3	1	1	1

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0 = control condition; 1= intervention condition

There are four, half yearly assessments. Each group consists of four or five YOD-SCU'S

Data collection and ethical considerations

The Beyond-II study protocol was approved by the Medical Ethics Committee region Arnhem/Nijmegen (file number 2015-1558) and registered in the Dutch Trial Register (Trial ID NTR5018). This research project was conducted according to the principles of the Declaration of Helsinki (version November 2013, www.wma.net) and in agreement with the laws regarding medical-scientific research in humans (WMO).

Written informed consent was obtained from the legal representative of each resident. After receiving informed consent, trained researchers and research assistants collected the data from the resident's medical files and through structured interviews with nursing staff members who were most involved in the daily care of the residents. No feedback was given to the nursing staff members during the assessments regarding the scores on the outcomes measures.

Primary outcome

The Dutch version of the Cohen-Mansfield Agitation Inventory (CMAI-D) was used to assess *agitation and aggression* [16, 41]. The CMAI has a well-established validity and reliability and assesses 29 agitated or aggressive behaviors [41]. The frequency of each symptom is rated on a seven-point frequency scale (range 1-7) ranging from never to several times an hour. We used CMAI factors based on a previous study in LOD in which three CMAI factors in a large NH sample were found: physically non-aggressive behaviors (range 7-49), physically aggressive behaviors (range 8-56), and verbally agitated behaviors (range 4-28) [42].

Secondary outcomes

To determine effects of the care program on *other NPS*, the Dutch version of the Neuropsychiatric Inventory-nursing home version (NPI-NH) was used. The NPI-NH has a high interrater reliability and is found to be a valid instrument for the assessment of a wide range of NPS in dementia [43, 44]. The NPI-NH consists of twelve NPS: delusions, hallucinations, agitation/aggression, depression, anxiety, euphoria, apathy/indifference, disinhibition, irritability/lability, aberrant motor behavior, nighttime behavior disturbances, and appetite/eating disturbances. For each symptom a screening question is used to determine whether the symptom is present. If the symptom is present, Frequency (F) and Severity (S) are rated on a four-point (ranging from 1-4) and three-point Likert-scale (ranging from 1-3), for each symptom, respectively. Scores for each symptom are calculated as F x S (ranging from 1-12). A symptom score of at least 4 is considered clinically relevant [45, 46].

PDU was derived from the nursing homes pharmacists' electronic files and was classified according to the Anatomical Therapeutic Chemical (ATC) classification system into antipsychotics, anxiolytics, hypnotics, antidepressants, anti-epileptics, anti-dementia drugs, and any psychotropic medication [47]. Pro re nata medication was not included because it was unclear if and how often these drugs were actually used. Furthermore, anti-epileptics used by residents with epilepsy were not registered as PDU.

Other measurements

Medical and demographic data were extracted from the resident's medical files. Data on dementia subtype, age, gender, length of stay at the SCU, and date of inclusion were recorded. *Dementia severity* was assessed with the Global Deterioration rating Scale (GDS) [48]. The GDS describes seven different stages of dementia on a seven-point scale (1-7), ranging from "subjectively and objectively normal cognition" to "severe cognitive decline".

Process data showed that the fidelity of the intervention (the degree to which the intervention was delivered as intended) differed between SCUs [30]. Differences between SCU's regarding fidelity will likely influence effectiveness of the intervention. Therefore, fidelity was conceptualized into an implementation score consisting of three components. A score was calculated for the step detection based on the number of times the step was completed with regard to the number of residents residing on the SCU (score 2 if used at least once every six months for 75-100% of all residents, score 1 if used for 50-74% , score 0 if used in < 50%) [30]. In addition, the NH staff rated the percentages of cases with challenging behavior in which they worked according to the care program on a questionnaire. A score was assigned to each SCU based on their answers (score 2 if used in 75-100% of the cases, score 1 if used in 50-74%, score

0 if used in < 50%). At last, two authors closely involved in the implementation (J. D. and B. A.) separately rated the implementation based on their communication with the SCUs (at least once every six months by telephone or email) about the progress of the implementation (ranging from 0-2, with a higher score indicating a higher degree of implementation). Disagreements were solved by discussion. The scores on the three components were summed, resulting in a total implementation score (ranging from 0 – 6).

Statistical analysis

All analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 22. Demographic variables of the NH residents at time of enrolment in the study were described by means or proportions. Before analysis, all data were checked for missing values. In the case of missing values, no data was imputed.

Multilevel model analyses were used to adjust for the clustering of residents in the thirteen different SCUs and the correlation of the repeated measures within the residents. The CMAI factor scores were checked for normality. The twelve symptom scores on the NPI-NH were dichotomized into clinical relevant symptoms (symptom score ≥ 4) or no clinical relevant symptoms (symptom score <4). Data on PDU was also dichotomized (present or absent) for each category (antipsychotics, anxiolytics, hypnotics, antidepressants, anti-epileptics, anti-dementia drugs, any psychotropic medication). In case of binary variables (like NPI-NH clinical relevant symptom scores and PDU), the fit for logistic and linear mixed model logistic regression were explored by comparing the observed and predicted profiles of SCUs over time. In the case of an equal or better fit, we used linear regression instead of logistic regression as this allows a direct interpretation in terms of change of percentage over time. ICCs were calculated from the variances at the three levels as follows:

$$\text{ICC } assesment = \frac{var\ scu + var\ resident}{var\ scu + var\ resident + var\ assessment} \quad \text{and ICC } resident = \frac{var\ scu}{var\ scu + var\ resident}$$

In a previous study evaluating the effect of the intervention in LOD (on which our intervention was based on), dementia severity and time being exposed to the intervention had an influence on the intervention effect [25]. In addition, differences in fidelity between SCUs could influence the intervention effect [30]. Therefore, to investigate whether the intervention effect was different for residents with more advanced dementia (GDS score <5 mild, score = 5 moderate, score ≥6 severe), or different for residents exposed to the intervention for a longer period of time (0-6 months, 6-12 months, 12-18 months), or different for a higher fidelity (implementation score), interaction effects between the intervention and these variables were investigated. In all analyses, a p value <0.05 was considered statistically significant.

Results

In total, 274 NH residents with YOD participated in this study. At time of inclusion, mean age was 64 years, and the male to female ratio was approximately equal (Table 2). The mean length of stay at the SCU was 28 months. The majority of residents (62.8%) had severe dementia. Most residents were diagnosed with AD (43.8%), followed by frontotemporal dementia (29.2%). One hundred and thirty-one residents participated in all assessments. Seventy-six residents were lost to follow-up because they moved to another care unit or deceased before the end of the study. Sixty-seven newly admitted residents were included after T0. Of the newly admitted residents after T0, baseline data on the outcome variables was not available in all cases. Those residents could at time of first assessment already have been exposed to the intervention for some months, depending on which group the SCU was assigned to (Table 1). Therefore, the number of residents with baseline data on outcome variables (n = 227) (Table 3) is lower compared to the number of residents participating in the study (n = 274) (Table 2). The most prevalent types of NPS (NPI-NH) were agitation/aggression and apathy. Sixty-seven percent used at least one psychotropic drug, with antidepressants being the most prevalent type (35.2%).

Table 2. Demographic and clinical characteristics of the nursing home residents at time of inclusion (n = 274).

Age	Mean (SD) [Range]	63.86 (5.91) [39-78]
Gender	Male n (%)	138 (50.40)
Length of stay at the SCU (months)[a]	Mean (SD) [Range]	28.65 (32.10) [1-259]
Dementia severity (GDS)[b]	n (%)	
Mild (2,3,4)		43 (15.70)
Moderate (5)		57 (20.80)
Severe (6,7)		172 (62.80)
Dementia subtype	n (%)	
Alzheimer' disease		120 (43.80)
Vascular dementia		29 (10.60)
Frontotemporal dementia		80 (29.20)
Mixed Alzheimer/vascular		14 (5.10)
Lewy Body/ Parkinson		5 (1.8)

Table 2 (no. 114) continued

Alcohol related dementia	6 (2.20)
Other	20 (7.30)

[a] 5 missing

[b] 1 missing

SD = Standard Deviation; SCU = Special Care Unit; GDS = Global Deterioration Scale

Table 3. Baseline data on outcome variables at the time of inclusion (n=227).

CMAI factor scores	Mean (SD)	
Physically aggressive behaviors		13.02 (6.41)
Physically nonaggressive behaviors		14.86 (7.90)
Verbally agitated behaviors		8.46 (5.90)
Clinical relevant NPI-NH	n (%) with Mean FxS (SD)	
Delusions		29 (12.80) 8.45 (2.87)
Hallucinations		29 (12.80) 6.86 (3.01)
Agitation/Aggression		95 (41.90) 7.27 (2.80)
Depression		42 (18.50) 7.29 (3.08)
Anxiety		33 (14.50) 8.18 (3.02)
Euphoria		23 (10.10) 8.04 (3.14)
Apathy		93 (41.00) 8.52 (3.28)
Disinhibition		69 (30.40) 8.07 (3.00)
Irritability		84 (37.00) 7.63 (2.63)
Aberrant motor behavior		89 (39.20) 8.47 (3.30)
Nighttime behavior disturbances		37 (16.30) 7.57 (2.97)
Eating disturbances		43 (18.90) 7.56 (2.86)

Table 3 (no. 114) continued

PDU	n (%)
Antipsychotics	71 (31.30)
Anxiolytics	60 (26.40)
Hypnotics	34 (15.00)
Antidepressants	80 (35.20)
Anti-epileptics	22 (9.70)
Anti-dementia drugs	12 (5.30)
Any psychotropic medication	152 (67.00)

SD = Standard Deviation; Mean F x S = mean frequency x severity scores of clinically relevant NPI-NH scores; PDU = psychotropic drug use
Only the scores for residents included at T0 and residents included at T1 or T2 which not yet had been exposed to the intervention are shown.

For all variables (including binary variables), linear regression models were used because these models had a better or equally good fit. The analyses showed no significant effect of the intervention on physically aggressive behaviors, physically non-aggressive behaviors, and verbally agitated behaviors (Table 4.). Additionally, no effect of the intervention on other NPS was found. A trend towards a decrease in the use of antidepressants after implementation of the intervention was found (Table 4).

Table 4. Effects of the intervention on NPS and PDU.

	Estimate	P	95% CI		ICC	ICC
			Lower bound	Upper bound	Assess-ment	Resi-dent
CMAI factor scores						
Physically non-aggressive behaviors	-.137	.825	-1.358	1.074	.616	.023
Physically aggressive behaviors	.495	.303	-.448	1.438	.681	.030
Verbally agitated behaviors	-.176	.697	-1.065	.713	.641	.011
Clinically relevant NPI-NH						
Delusions	-.048	.136	-.111	.015	.104	.041
Hallucinations	.044	.135	-.014	.101	.094	.044

Table 4 (no. 115) continued

Agitation/aggression	-.001	.975	-.090	.087	.238	.108
Depression	.022	.560	-.052	.096	.137	.052
Anxiety	.034	.318	-.033	.102	.123	.053
Euphoria	.031	.338	-.033	.095	.104	.034
Apathy	.051	.320	-.051	.154	.240	.077
Disinhibition	.077	.092	-.013	.167	.191	.066
Irritability-	.000	.999	-.087	.087	.230	.099
Aberrant motor behavior	.049	.284	-.041	.139	.236	.110
Nighttime behavior disturbances	.050	.180	-.023	.122	.034	.239
Eating disturbances	.044	.253	-.031	.118	.156	.071
PDU						
Antipsychotics	-.002	.956	-.064	.060	.225	.171
Anxiolytics	-.033	.301	-.095	.029	.188	.133
Hypnotics	-.021	.459	-.078	.035	.118	.070
Antidepressants	-.057	.066	-.117	.004	.118	.070
Anti-epileptics	.029	.126	-.008	.067	.109	.097
Anti-dementia drugs	-.005	.781	-.045	.044	.047	.029
Any psychotropic medication	-.023	.505	-.090	.044	.222	.163

PDU = psychotropic drug use

No significant interaction effects between dementia severity and fidelity and the intervention effect were found. A significant interaction effect for the effect of the intervention and the time that a resident was exposed to the intervention with regard to the prevalence of delusions was found (p = .024). After being exposed for a longer period of time to the intervention it became more effective in decreasing delusions, with an estimated intervention effect of -.06 (p = .056) for SCUs which worked 0-6 months with the intervention to an estimated intervention effect of -.06+2*-.06 (estimated intervention effect = -.18, p =0.08) for SCUs working 12-18 months with the intervention.

Discussion

To our knowledge, this is the first study that evaluated the effects of a multidisciplinary intervention on the management of NPS in NH residents with YOD on the presence of NPS, particularly agitation and aggression, and PDU. The intervention was not more effective in reducing agitation and aggression, other NPS, or PDU compared to care as usual.

In contrast, other studies into the management of NPS in dementia resulted in significant reduction of NPS. However, these studies cannot be directly compared to this study, because these studies made a preselection of residents with clinical relevant/severe NPS (based on a cut-off score or selected by NH staff) [49-52]. The current study is implemented on SCU level, which means all residents receive the intervention. Consequently, analysis was done on all residents, which might have diluted the possible effects.

Nonetheless, the intervention for the management of NPS and PDU in LOD, on which our intervention was based on, was also implemented on unit level and still effectiveness was established [25]. An explanation for the differences in effects between the original intervention and the adapted intervention for YOD might be that all participating SCUs in our study were recruited through NHs that were affiliated with the Dutch YOD Knowledge Center (DKC). This knowledge center aims to improve the quality of care for people with YOD by developing specific guidelines, supporting scientific research, and implementing research findings in clinical practice. Only care organizations offering specialized care for people with YOD are affiliated with the center. Those organizations are familiar with the specific needs of younger residents. Therefore, they might have already (to some degree) developed effective working methods for the management of NPS in YOD before implementation of our intervention [12-14]. Indeed, the process evaluation that was performed alongside implementation of the intervention revealed that the NH staff experienced overlap between the intervention and their current working methods [30]. In addition, steps of the intervention, like detection and tool to monitor PDU, were often rated as irrelevant [30]. This suggests that users of the intervention did not expected that these steps would be more effective in diminishing NPS and PDU compared to care as usual in YOD SCUs. Possibly, in YOD SCUs there was less need for an intervention which structured the management of NPS compared to LOD care units. The needs from one setting (LOD care units) cannot be completely generalize to another setting (YOD SCUs). During the development phase of the intervention, research on the specific needs and context of YOD SCUs (like pilot study, focus group with YOD NH staff) could have improved implementation.

Despite adding a tool to the intervention for monitoring PDU, no significant

decrease in PDU after implementation of the intervention was found. A possible explanation could be that the current policy that favors limiting the prescription of psychotropic drugs, has already positively influenced the prescription pattern to some degree, leaving fewer room for improvement [53]. Indeed, when comparing the PDU rates in our study (68.6 % using at least one drug) with the PDU rates in NH residents with YOD approximately 10 years ago (87.6 % using at least one drug), the PDU rates in our study appear considerably lower [4].

Our results suggest that after working longer with the intervention, it became more effective in decreasing delusions. However, the time that a resident was exposed to the intervention did not have an influence on the intervention effect for other NPS. Not even a trend towards in- or decreasing effectiveness was found for other NPS. Therefore, we expected that this interaction effect might have been a result of multiple testing.

This study has several strengths. We were able to include a large sample size of NH residents, resulting in sufficient study power. This is an advantage especially in research on YOD, because the prevalence of NH residents with YOD is much lower compared to LOD. Moreover, besides effect analysis, a process evaluation was performed to provide qualitative data about validity, the implementation strategy, and contextual factors affecting implementation [30]. This process information provided important knowledge about which factors needed to be taken into account during effect analysis. Furthermore, it helped to understand why the intervention was ineffective and which adaptations have to be made to increase relevance and fidelity of the intervention [31, 54]. Also, some limitations of this study should be considered. The presence of NPS was based on observations of nurses who could not be blinded. Awareness of being in the intervention or control condition might have influenced their ratings to some degree. Furthermore, no assessment instruments are available which take into account the specific characteristics of younger individuals with dementia. Therefore, we chose to measure NPS with assessment instruments (NPI-NH, CMAI) designed and validated for the use in NH residents with LOD [41, 43]. However, especially the CMAI does not extensively assess behavior associated with frontal lobe dysfunction, which might be more likely to occur in younger NH residents with dementia because of the higher prevalence of FTD [1]. Therefore, some caution should be used when interpreting our findings.

Conclusions

The intervention was not more effective in reducing agitation and aggression, other NPS, or PDU compared to care as usual. The perceived overlap between the intervention and their current working methods and the lower PDU rates compared to approximately 10 years ago, suggests that YOD SCUs have already (to some degree) developed effective working methods for structuring the management of NPS in YOD before implementation of our intervention, diminishing the intervention effect. In future studies, more research on the specific needs and context of YOD SCUs during the development phase of an intervention is important to improved relevance and effectiveness of an intervention in this specific context.

References

1. Mulders AJMJ, Zuidema SU, Verhey FR, Koopmans RTCM: Characteristics of institutionalized young onset dementia patients – the beyond study. International Psychogeriatrics 2014;12:1973–1981.
2. Murman DLD, Chen Q, Powell MC, et al.: The incremental direct costs associated with behavioral symptoms in AD. Neurology 2002;59:1721-1729.
3. Wetzels R, Zuidema S, de Jonghe JF, Verhey FJ, Koopmans, RTCM: Determinants of quality of life in nursing home residents with dementia. Dementia and Geriatric Cognitive Disorders 2010;29:189-197.
4. Mulders AJMJ, Fick IWF, Bor H, et al.: Prevalence and correlates of neuropsychiatric symptoms in nursing home patients with young-onset Dementia: The BEYOnD Study. Journal of the American Medical Directors Association 2016; 17: 495-500.
5. Zwijsen SA, Kabboord A, Eefsting JA, et al.: Nurses in distress? An explorative study into the relation between distress and individual neuropsychiatric symptoms of people with dementia in nursing homes. International Journal of Geriatric Psychiatry 2014; 29:384-391.
6. Appelhof B, Bakker C, van Duinen-van den IJssel JCL, et al.: The determinants of quality of life of nursing home residents with young-onset dementia and the differences between dementia subtypes. Dementia and geriatric cognitive disorders 2017;43:320–329.
7. van Duinen-van den IJssel JCM, Mulders AJMJ, Smalbrugge M, et al.: Nursing Staff Distress Associated With Neuropsychiatric Symptoms in Young-Onset Dementia and Late-Onset Dementia. Journal of the American Medical Directors Association 2017;Epub ahead of print.
8. Appelhof B., Bakker C, van Duinen-van den IJssel JCL, et al.: Differences in neuro-psychiatric symptoms between nursing home residents with young-onset dementia and late-onset dementia. Aging and Mental Health 2018;Epub ahead of print.
9. Wetzels RB, Zuidema SU, De Jonghe JFM, Verhey FRJ, Koopmans RTCM: Prescribing pattern of psychotropic drugs in nursing home residents with dementia. International Psychogeriatrics 2011;23(8):1249-59.
10. Ballard C, Howard R: Neuroleptic drugs in dementia: benefits and harm. Nature Reviews Neuroscience 2006;7(6):492-500.
11. Schneider LS, Dagerman K, Insel PS: Efficacy and adverse effects of atypical antipsychotics for dementia: meta-analysis of randomized, placebo-controlled trials. American Journal of Geriatric Psychiatry 2006;14(3):191-210.

12. Nederlands Instituut van Psychologen (NIP): Handreiking Psychologische hulpverlening bij gedragsproblemen bij dementie, Amsterdam, NIP, SPO, 2013.
13. Verenso: Richtlijn Probleemgedrag bij mensen met dementie, Verenso, 2018.
14. Verpleegkundigen & Verzorgenden Nederland (V&VN): Richtlijn omgaan met gedragsproblemen bij patiënten met dementie, Nijmegen, V&VN, 2005.
15. Cohen-Mansfield JJ: Nonpharmacologic interventions for inappropriate behaviors indementia: a review, summary, and critique. The American journal of geriatric psychiatry : official journal of the American Association for Geriatric Psychiatry 2001;9(4):361-81.
16. Cohen-Mansfield J, Billig N: Agitated behaviors in the elderly. I. A conceptual review. Journal of the American Geriatrics Society 1986;34:711–21.
17. Cohen-Mansfield JJ: Heterogeneity in dementia: challenges and opportunities. Alzheimer Disease and Associated Disorders 2000;14(2):60-3.
18. Kovach CR, Noonan PE, Schlidt AM, Wells T: A model of consequences of need driven, dementia-compromised behavior. Journal of nursing scholarship : an official publication of Sigma Theta Tau International Honor Society of Nursing / Sigma Theta Tau 2005;37(2):134-40.
19. Edvardsson D, Winblad B, Sandman PO: Person-centred care of people with severe Alzheimer's disease: current status and ways forward. The Lancet Neurology 2008;7(4):362-7.
20. Bakker C, de Vugt ME, van Vliet D, et al.: The relationship between unmet care needs in young-onset dementia and the course of neuropsychiatric symptomps: a two year follow-up study. International Psychogeriatrics 2014;26(12):1991–2000.
21. Koopmans RCTM, Pellegrom M, van der Geer ER: The Dutch Move Beyond the Concept of Nursing Home Physician Specialists. Journal of the American Medical Directors Association 2017; Epub ahead of print.
22. Ribbe MW, Ljunggren G, Steel K, et al.: Nursing homes in 10 nations: a comparison between countries and settings. Age and Ageing 1997;26:3-12.
23. Zwijsen SA, Smalbrugge M, Zuidema SU, et al.: Grip on challenging behaviour: a multidisciplinary care programme for managing behavioural problems in nursing home residents with dementia. Study protocol. BMC Health Services Research 2011;11(41):1-6.
24. Zwijsen SA, Gerritsen DL, Eefsting JA, et al.: The development of the Grip on Challenging Behaviour dementia care programme. International journal of palliative nursing 2014;20(1):15-21.

25. Zwijsen SA, Smalbrugge M, Eefsting JA, et al.: Coming to grips with challenging behavior: a cluster randomized controlled trial on the effects of a multidisciplinary care program for challenging behavior in dementia. Journal of the American Medical Directors Association 2014;15(7):531.
26. Zwijsen SA, Gerritsen DL, Eefsting JA, et al.:Coming to grips with challenging behaviour: a cluster randomised controlled trial on the effects of a new care programme for challenging behaviour on burnout, job satisfaction and job demands of care staff on dementia special care units. International journal of nursing studies 2015;52(1):68-74.
27. Orrell M, Hancock G: CANE: Camberwell Assessment of Need for the Elderly, Gaskell, 2004.
28. van der Spek K, Gerritsen DL, Smalbrugge M, et al.: A reliable and valid index was developed to measure appropriate psychotropic drug use in dementia. Journal of clinical epidemiology 2015;68(8):903-12.
29. van Duinen-van den IJssel JCL, Appelhof B, Zwijsen SA, et al.: Behavior and Evolution of Young-ONset Dementia part 2 (BEYOND-II) study: an intervention study aimed at the improvement of the management of challenging behavior in institutionalized people with young-onset dementia. International Psychogeriatrics 2017; Epub ahead of print.
30. Appelhof B, Bakker C, van Duinen-van den IJssel JCL, et al.: Process evaluation of an intervention for the management of neuropsychiatric symptoms in institutionalized people with young-onset dementia: the Beyond-II study. Journal of the American Medical Directors Association 2018;30(3):437-446.
31. Leontjevas R, Gerritsen DL, Koopmans RTCM, Smalbrugge M, Vernooij-Dassen MJ: Process evaluation to explore internal and external validity of the “Act in Case of Depression” care program in nursing homes. Journal of the American Medical Directors Association 2012;13:448e481-448e488.
32. American Psychiatric Association: Diagnostic and statistical manual of mental disorders- text revision: DSM-IV-TR. Washington DC, American Psychiatric Association, 2000,vol 1,pp 943.
33. Gorno-Tempini ML, Hillis AE, Weintraub S, et al.:Classification of primary progressive aphasia and its variants. Neurology 2011;76:1006-1014.
34. McKeith IG: Consensus guidelines for the clinical and pathologic diagnosis of dementia with lewy bodies (dlb): Report of the consortium on dlb international workshop. Journal of Alzheimer’s Disease 2006;9:417-423.

35. McKhann G, Drachman D, Folstein M, et al.: Clinical diagnosis of alzheimer's disease: Report of the nincds-adrda work group under the auspices of department of health and human services task force on alzheimer's disease. Neurology 1984;34:939 944.

36. Rascovsky K, Hodges JR, Knopman D, et al.: Sensitivity of revised diagnostic criteria for the behavioural variant of frontotemporal dementia. Brain : a journal of neurology 2011;134:2456-2477.

37. Roman GC, Tatemichi TK, Erkinjuntti T, et al.: Vascular dementia: Diagnostic criteria for research studies. Report of the ninds-airen international workshop. Neurology 1993;43:250-260.

38. van der Spek K, Gerritsen DL, Smalbrugge M, et al.: A reliable and valid index was developed to measure appropriate psychotropic drug use in dementia. Journal of Clinical Epidemiology 2015; 68(8): 903-912.

39. van der Spek K, Gerritsen DL, Smalbrugge M, et al.: PROPER I: frequency and appropriateness of psychotropic drugs use in nursing home patients and its associations: a study protocol. BMC Psychiatry 2013;13:1-7.

40. Brown CA, Lilford RJ: The stepped wedge trial design: a systematic review. BMC Medical Research Methodology 2006;6:54.

41. de Jonghe JF, Kat MG: Factor structure and validity of the Dutch version of the Cohen Mansfield Agitation Inventory (CMAI-D). Journal of the American Geriatrics Society 1996;44:888-889.

42. Zuidema SU, de Jonghe JF, Verhey F R, Koopmans RCTM: Agitation in Dutch institutionalized patients with dementia: factor analysis of the Dutch version of the Cohen-Mansfield Agitation Inventory. Dementia and Geriatric Cognitive Disorders 2007;23:35-41.

43. Kat MG, de Jonghe JF, Aalten P, et al.: Neuropsychiatric symptoms of dementia: Psychometric aspects of the dutch neuropsychiatric inventory (npi). Tijdschrift voor Gerontologie en Geriatrie 2002;33:150-155.

44. Kaufer DI, Cummings JL, Ketchel P, et al.: Validation of the NPI-Q, a brief clinical form of the Neuropsychiatric Inventory. J Neuropsychiatry Clin Neurosci 2000;12:233-239.

45. Wood S, Cummings EL, Hsu MA, et al.: The use of the neuropsychiatric inventory in nursing home residents. Characterization and measurement. American Journal of Geriatric Psychiatry 2000;8:75-83.

46. Zuidema SU, Derksen E, Verhey FR, Koopmans RT: Prevalence of neuropsychiatric

symptoms in a large sample of Dutch nursing home patients with dementia. International Journal of Geriatric Psychiatry 2007;22(7):632-638.

47. WHO: Anatomical therapeutical chemical (atc) classification index including defined daily doses (ddds) for plain substances. Oslo, World Health Organisation Collaborating Centre for Drug Statistics Methodology, 1997.

48. Reisberg B, Ferris SH, de Leon MJ, Crook T: The global deterioration scale for assessment of primary degenerative dementia. The American Journal of Psychiatry 1982;139:1136–1139.

49. Pieper MJC, van der Steen JT, Francke AL, et al.: Effects on pain of a stepwise multidisciplinary intervention (STA OP!) that targets pain and behavior in advanced dementia: A cluster randomized controlled trial. Palliative Medicine 2018;32(3):682 692.

50. Chenoweth L, King MT, Jeon YH, et al.: Caring for Aged Dementia Care Resident Study (CADRES) of person-centred care, dementia-care mapping, and usual care in dementia: a cluster-randomised trial. The Lancet Neurology 2009;8(4):317-325.

51. Opie J, Doyle C, O'Connor DW: Challenging behaviours in nursing home residents with dementia: a randomized controlled trial of multidisciplinary interventions. International Journal of Geriatric Psychiatry 2002;17(1):6-13.

52. McCabe MP, Bird M, Davison TE, et al.: An RCT to evaluate the utility of a clinical protocol for staff in the management of behavioral and psychological symptoms of dementia in residential aged-care settings. Aging and Mental Health 2015;19(9):799 807.

53. Smeets CHW, Smalbrugge M, Zuidema SU, et al.: Factors related to psychotropic drug prescription for neuropsychiatric symptoms in nursing home residents with dementia. Journal of the American Medical Directors Association. 2014;15(11):835-840.

54. Bonell C, Fletchter A, Morton M, Lorenc T, Moore L: Realist randomised controlled trials: A new approach to evaluating complex public health interventions. Social Science & Medicine 2012;75:2299-306.

6


Family
I'm glad I
I love you
I wish I could remember
Pain
New challe
help
happiness
love
love life
how
Take care of the children
I forgot
I don't know
Golden years
enjoy
Good life
Work
learning
why
angry
I have
Friends
to grow
away from home
the beginning

Chapter 7

GENERAL DISCUSSION

This thesis is part of the BEYOND-II study. In this study, a multi-component intervention for the management of neuropsychiatric symptoms (NPS) in institutionalized people with young-onset dementia (YOD) was developed. The aim of this thesis was to provide knowledge to further improve specialized long-term care for people with YOD. The first part of this thesis focuses on consequences of NPS for the quality of life (QoL) of residents with YOD and differences in NPS between residents with YOD and late-onset dementia (LOD) (Chapters 2 and 3). In the second part of this thesis, the development, implementation process, and effects of the intervention on NPS and psychotropic drug use (PDU) are described (Chapters 4, 5, and 6). This general discussion provides a summary of the main findings of this thesis. Methodological considerations will be discussed. In addition, the findings of this thesis will be considered within the context of daily practice and recommendations for future research will be given.

Summary of the main findings

1. *What are the determinants of quality of life of NH residents with YOD and are there differences between dementia subtypes regarding these determinants?*

We found that residents' QoL was negatively associated with advanced dementia, PDU, agitation and aggression, depression, and apathy. In addition, aspects of QoL differed by dementia subtype. Residents with FTD showed fewer negative emotions, were more inclined to accept help, experienced better quality of relationships with professional caregivers, had a more positive self-image, and felt more comfortable in the NH environment compared to residents with AD or vascular/mixed dementia. On the contrary, residents with FTD appeared to experience a lower quality in their social relationships.

2. *Are there differences in NPS between NH residents with YOD and LOD and can these possible differences be attributed to differences in dementia subtype, gender, psychotropic drug use, or dementia severity?*

No differences in NPS rates between NH residents with YOD and LOD were found, except for apathy. Furthermore, higher levels of PDU in YOD compared to LOD were found, irrespective of the presence of NPS.

3. *Are internal and external validity of a multi-component intervention for the management of NPS in NH residents with YOD sufficient and what are barriers and facilitators for implementation of the intervention?*

A process evaluation showed sufficient internal and external validity, allowing for further effect analyses of the intervention for the management of NPS in YOD. Staff turnover and

shortages, organizational changes, lack of involvement in the educational program, and overlap with current working methods were perceived as important barriers for implementation by the multidisciplinary team. Facilitators that were mentioned involved multidisciplinary collaboration, limited involvement in other projects, openness to change in working procedures, and the support of the ambassador and management. Despite an enhanced implementation strategy aimed at overcoming barriers already identified in previous implementation studies [1-3], in none of the SCUs all steps of the intervention were completely carried out as planned.

4. *What is the effect of a multi-component intervention on the prevalence of NPS (particularly agitation and aggression) and PDU in residents with YOD compared to care as usual?*

No decrease in agitation and aggression, other NPS, and PDU was found after implementation of the intervention. Overlap between the intervention and working methods already used before implementation, might have diminished the intervention effect.

Methodological considerations

Some methodological considerations of this study should be discussed. To be able to compare our results with earlier studies on YOD (the Beyond study and the NeedYD study) [4, 5], we excluded residents with a symptom onset after the age of 65, traumatic brain injury, Korsakov syndrome, Huntington's disease, human immunodeficiency virus (HIV), or Down syndrome. However, there is no international consensus on the definition of YOD [6]. The cut-off at age 65 is considered arbitrary as this is only based on the social division in terms of employment and retirement age. Other differences between younger and older people with dementia (like differences in social network, family structure, vitality, etiology) are not taken into account [6]. In order to provide consensus on an operational definition of YOD, the Prevalence REcognition and Care pathways in young Onset Dementia (Precode) study recently started [7]. Also, admission criteria for YOD SCUs differ between health care organizations. In some YOD SCUs a YOD diagnosis is not a requirement for admission. Placement depends on other factors like social characteristics or somatic care needs. Consequently, in some of the participating SCUs in this study less than fifty percent of the residents were eligible for inclusion. Therefore, we should be aware that the results of this study cannot be generalized to all people residing on YOD SCUs.

Furthermore, we did not perform all steps from the Medical Research Council (MRC) framework as a guide for adapting the original intervention for the use in YOD SCUs [8].

Information on perceived barriers and facilitators for implementation found in previous studies on LOD units was used to develop the intervention and implementation strategy in this study [1-3]. However, during the course of the study we became aware that results from one setting (LOD care units) could not be transferred to another setting (YOD SCUs) completely. For example, in our study overlap between the intervention and current working methods was mentioned as a barrier for implementation, while the LOD NH staff did not experience this particular barrier. This implies that YOD SCUs were more inclined to already, at least to some degree, use a structured working method for the management of NPS, limiting the relevance of some steps of the intervention. According to the MRC framework, additional research on the specific context of YOD SCUs (like interviews, a pilot study, or a focus group with YOD NH staff) during the development phase of the intervention and the development of the implementation strategy, could have further improved the relevance and fidelity of the intervention in this specific context [8].

At last, The Dutch National Health Care Institute, which determines and advises on in- and exclusion of different types of health care in the basic care package, wrote a report on the complexity of establishing effect of an intervention in long-term care [9]. Although a randomized controlled trial (RCT) is widely considered as the golden standard for providing evidence for the effectiveness of clinical trials and is the best method to minimize selection bias and to determine intervention effects, it is important to take into account its limitations for complex interventions in long-term care [9,10]. The intervention in this thesis can be considered complex because of the different interacting components of the intervention (five-step care program and the educational program) and the diversity in NH staff members using the intervention [8] (Chapter 4). First, in RCTs contextual factors are often perceived as influences that need to be controlled for, in order to isolate the intervention effect [9]. A RCT does not examine how complex interventions interact within the context in which they are implemented and received [11]. However, according to the realism approach, contextual factors are part of daily practice and therefore RCT's often do not reflect the real clinical environment. Realists state that it is not the intervention by itself, but the interaction of the intervention with the context that is the core of change [10]. Therefore, contextual information is necessary to understand why an intervention was (in)effective in a specific setting and to successfully reproduce the intervention in another setting. In order to overcome this limitation, along with effect analysis a process evaluation was performed to provide qualitative data about the implementation strategy and contextual factors affecting implementation (Chapter 5). Secondly, RCTs fail to understand the effects of intervention components separately in order to make conclusions about

which specific intervention components are effective within a context and which specific components are redundant or need adjustment [11]. This could be resolved by using multi-arm studies in which various steps of the intervention are investigated in different arms [10]. However, this approach only works if the intervention components are non-interacting, which was not the case in our study [10]. In order to be able to provide some information about the specific intervention components in this study, qualitative data about the relevance and feasibility perceived by the users of the intervention of each step of the intervention was collected (Chapter 5). This information provided important insight into the adaptations which have to be made to increase relevance and fidelity of the intervention. Thirdly, RCTs are perceived to be double-blinded: neither NH staff nor residents should be aware if they are in the control or intervention condition. However, this assumption is often violated in a complex intervention in long-term care [9, 11]. Also, in this study, NH staff was aware that they were in the intervention condition because that condition required working with the intervention. To minimize bias, no feedback was given to the nurses during the assessments regarding the scores on the outcome measures.
To overcome lack of blinding in future complex intervention studies, a solution could be to assess the outcome variables with observations of research assistants blind to intervention allocation. Furthermore, the use of a factorial design, in which SCUs are randomly allocated to one or more interventions simultaneously using various combinations of interventions, makes it more straightforward to maintain blinding [12, 13].

Clinical implications

This thesis provides important clinical implications for care giving in NH residents with YOD and future implementation of interventions in NHs. The higher rates of apathy in YOD (Chapter 3) raise concern because of the strong association with QoL of the residents (Chapter 2). Moreover, apathy has found to be an important predictor for institutionalization, has been found related to mortality of NH residents with dementia, and has been found associated with high levels of informal caregiver distress in community-dwelling people with dementia [14-16]. Although not yet investigated, it is expected that the same association between apathy and distress applies to informal caregivers of NH residents with dementia. These results underscore the need for adequate detection and treatment of apathy especially in residents with YOD. Despite the increased interest in the treatment of apathy in dementia, results of intervention studies in LOD are inconsistent and still no effective treatment has yet been established [17-20]. However, the results of cognitive stimulation and activation strategies on apathy in dementia are promising [21-22],

suggesting that proving mentally stimulating activities can decrease apathy. Research in community-dwelling people with YOD found that a feeling of being engaged and feeling useful is important when offering activities to people with YOD [25]. Therefore, household activities, work-related activities, and social activities might be important to at least community-dwelling people with YOD. This is in line with the concept of social health which focuses on the capacity and potential of the person with dementia in order to prevent disengagement and improve self-manage, instead of focusing on symptoms and disability [24, 25]. Important research has been done on social health in NH residents with LOD providing new opportunities for people with dementia to participate in social life [26, 27]. More research is needed to explore what type of activities meet the needs of NH residents with YOD and to investigate the effects of activities on decreasing apathy. Also, to increase awareness and insight in apathy in NH residents with YOD, in the detection of NPS in clinical practice and in future research on YOD apathy should be more extensively assessed by using specific tools like the Apathy Evaluation Scale [28].

The heterogeneity of the YOD NH population implies that a distinction between placement on a YOD or LOD unit purely based on age of symptom onset (before or after the age of 65) is an oversimplification. The high proportions of less common causes of dementia in YOD (such as FTD) with different care needs with regard to QoL (Chapter 2) and the highly variable age of NH residents with YOD [range 39-78 years] demands flexibility in care skills, day time activities, support, and physical environment. By placing people on a YOD SCU only based on age of symptom onset, the resident's individual care needs might be overlooked. Over the last decade, several Dutch NHs introduced sociotherapeutic living environments. In a sociotherapeutic living environment, the supply of care, therapeutic guidance, daily activities and housing are methodically coordinated, in order to achieve the best possible quality of life. Within one care-organization different living groups can be organized, based on residents' social, psychological and physical care needs [29]. The Dutch YOD Knowledge Center (DKC) already acknowledges the importance of sociotherapeutic living environments and facilitates the use by providing a guideline for the implementation on YOD SCUs [30]. However, no research has been done on the effectiveness of sociotherapeutic living environments in clinical practice. Currently, the Netherlands Organization for Health Research and Development provides funding to optimize implementation and investigate the effect of sociotherapeutic living environments in Dutch NHs on QoL, NPS, and PDU in residents with dementia (LIVE-study-ZonMW project number 733050708) [31]. The results of this study might be useful to also further improve individualized care in residents with YOD.

Furthermore, our results raise awareness of the difficulties with implementation of standardized complex intervention within different settings. In none of the YOD SCUs all steps of the intervention were completely carried out as planned. Other implementation studies in NHs also faced implementation barriers [6, 7, 11, 32, 33]. Although standardized interventions and protocols provide a definition of good quality of care, enable evidence-based treatment, and facilitate comparison of quality of care between services, they are unable to take into account all contextual influences. For example, on some small-scale units or units with a low nursing staff-resident ratio, it was impossible to fill in the analysis of NPS (step of the intervention) with a colleague like the intervention prescribes, therewith hindering implementation. A second-best solution to improve quality of care could be to allow for more customization of the intervention to the contexts of a specific settings. This can be achieved by performing participatory action research (PAR) [34]. In PAR the participants (in this study NH staff) would be actively involved in the collection and analysis of data about the specific context. Based on this information the participants determine which actions should follow. Experiences from a PAR study on improving antimicrobial prescribing showed that participants appreciated being involved in the development and implementation of an intervention. Also, in this study different interventions were selected by the participants for different settings, which strengthens the assumption that a 'one size fits all' approach is not the best solution to improve quality of care [35]. A recent example of PAR in the management of NPS in dementia is 'the Reduction of Inappropriate psychotropic Drug use in NH residents with dementia (RID) study', in which for each NH the prescription pattern of psychotropic drugs was analyzed together with the NH staff [36]. Researchers provided a list of several possible interventions for optimizing the prescription pattern. Based on their analysis, the NH staff chose which intervention had the most potential in the specific context of their NHs. The results of this study are expected in 2019.

Currently, a similar discussion about the feasibility of implementing standardized interventions and protocols within different contexts arose when the Dutch government presented a plan of action to improve the quality of NH care in the Netherlands [37]. Although there was agreement on the conditions necessary to provide good care between NHs, like person-centered care, professional education and training, safety, learning and improving, sufficient and competent NH staff, NH staff asked for more flexibility in the methods to accomplish these conditions. The plan of action restricted the NH staff to develop working methods that suited the specific context of the own organization, therewith hindering improvement of care. To address this issue, the Dutch Ministry of Health, Welfare, and Sport (VWS) supported a pilot called 'Radicale Vernieuwing' in which

fifty-two NHs were allowed to develop their own working methods for good quality of care, regardless of current protocols [38]. The results of the pilot of VWS (presented in 2019) will provide more insight on the effects of a more flexible approach with regard to protocols and interventions on overall quality of NH care.

Future research directions

Several implications for future research in YOD emerge from the results of this thesis. First, more research is needed on adequate treatment of apathy in NH residents with YOD. Research on social health in LOD offers a promising starting point for the development of interventions which aim to improve social participation and self-manage [24]. More research is needed on the specific needs of NH residents with YOD regarding meaningful activities and the effects of these activities on the presence of apathy.

Furthermore, because of the heterogeneity of the YOD NH population, in future research on YOD there should be more differentiation between YOD and LOD than a distinction purely based on age of symptom onset. A solution could be to include large samples of NH residents with YOD and LOD combined in which subgroups based on age are created (for example youngest <45, young <65, old > 65, oldest > 90). Moreover, more research on specific subgroups like people with FTD is recommended, like the study of Prins and Hendriks on focusing in FTD [39].

At last, the lower PDU rates in NH residents with YOD compared to approximately 10 years ago are promising [5]. However, the current prescription rates of psychotropic drugs in NH residents with YOD remain high and seem still higher compared to LOD (Chapter 3). This suggests that the threshold for the use of psychotropic drugs in the management of NPS maybe lower in YOD compared to LOD. An explanation could be that NPS in younger individuals are perceived as more threatening or distressing by the nursing staff. Consequently, physicians might be more inclined to prescribe psychotropic drugs in YOD than in LOD [40]. Indeed, a recent study on the association between NPS and nursing staff distress in YOD and LOD showed that LOD nurses less often appeared to experience high levels of distress [41]. Another explanation could be that physicians are more concerned for poor health outcomes associated with PDU (like stroke, increased mortality) in older people with dementia [42,43]. In order to understand the differences in prescription pattern between YOD and LOD and therewith be able to further improve the psychotropic drug prescription pattern in YOD, research on the factors associated with PDU in YOD is needed.

Conclusions

This thesis provides valuable knowledge to further improve specialized long-term care for people with YOD. With regard to the determinants of QoL and presence of NPS there are a lot of similarities between NH residents with YOD and LOD, suggesting that NH residents with YOD and LOD should not be treated as two completely separate entities. Nonetheless, higher rates of apathy and its negative influence on QoL underscore the need for adequate detection and treatment of apathy especially in NH residents with YOD. Furthermore, the heterogeneity of the YOD NH population with regard to etiology and age demands flexibility in care skills, day time activities, support, and physical environment to meet the large variety in needs. In order for the NH staff to be able to address this large diversity of care needs of all residents with YOD, placement on a specific unit should depend on more factors then age of disease onset by itself.

With regard to establishing effectiveness of a complex intervention in daily practice, this thesis underscores the need for collecting qualitative data (focus groups, interviews, pilot study) in addition to quantitative data (RCT). Qualitative data in the development phase of the intervention and implementation strategy is necessary to attune the intervention to needs and context of a specific setting therewith improving relevance and fidelity of the intervention. In addition, qualitative data can provide knowledge about which specific intervention components are effective and which specific components are redundant or need adjustment. Moreover, qualitative data is necessary to understand how an intervention works within a context and how the context affects implementation.

At last, we should be aware of the difficulties for implementation of protocols and interventions in the context of daily practice. We should consider the feasibility of completely carrying out a standardized protocol or intervention as planned within different contexts. Implementation and effectiveness could improve by allowing for more customization of the intervention to the context of a specific setting.

References

1. Zwijsen SA, Kabboord A, Eefsting JA, et al.: Nurses in distress? An explorative study into the relation between distress and individual neuropsychiatric symptoms of peoplec with dementia in nursing homes. International Journal of Geriatric Psychiatry 2014; 29: 384-391.
2. Mentes JC, Tripp-Reimer T: Barriers and facilitators in nursing home intervention research. Western Journal of Nursing Research 2002;24(8):918-36.
3. van de Ven G, Draskovic I, Adang EMM, et al.: Effects of dementia-care mapping on residents and staff of care homes: a pragmatic cluster-randomised controlled trial. PLoS One 2013;8(7):1-7.
4. Zwijsen SA, Smalbrugge M, Eefsting JA, et al.: Grip on challenging behavior: process evaluation of the implementation of a care program. Trialsjournals 2014; 15: 2-11.
5. Mulders AJMJ, Fick IWF, Bor H, et al.:Prevalence and correlates of neuropsychiatric symptoms in nursing home patients with young-onset dementia: The beyond study. JAMDA 2016;17:495-500.
6. Koopmans R, Rosness T: Young onset dementia-what does the name imply? International Psychogeriatrics 2014;26(12):1931-1933.
7. UKON: Precode. Retrieved from http://ukonnetwerk.nl/Precode.
8. Craig P, Dieppe P, Nazareth I, Petticrew M: Developing and evaluating complex interventions: the new Medical Research Council guidance. BMJ 2008;337:1-6.
9. The Dutch National Health Care Institute: Passend onderzoek effectiviteit langdurige zorg. 2016, retrieved from https://www.zorginstituutnederland.nl/publicaties/rapport/2016/12/15/passend-onderzoek-effectiviteit-langdurige-zorg.
10. Marchal B, Westhorp G, van Belle S, et al.: Realist RCTs of complex interventions - an oxymoron. Social Science and Medicine 2013; 94: 124-8.
11. Bonell C, Fletchter A, Morton M, Lorenc T, Moore L: Realist randomised controlled trials: A new approach to evaluating complex public health interventions. Social Science & Medicine 2012;75:2299-306.
12. Ballard C, Orrell M, YongZhon, S, et al.: Impact of antipsychotic review and nonpharmacological intervention on antipsychotic use, neuropsychiatric symptoms, and mortality in people with dementia living in nursing homes: a factorial cluster randomized controlled trial by the well being and health for people with dementia (WHELD) program. Am J Psychiatry 2016;173: 252–262.
13. Cipriani A, Barbui C: What is a factorial trial? Epidemiology and Psychiatric Sciences 2013;22(3):213-215.

14. Nijsten JMH, Leontjevas R, Pat-El R, et al.: Apathy: Risk Factor for Mortality in Nursing Home Patients. Journal of the American Geriatrics Society 2017;65(10): 2182-2189.
15. De Vugt ME, Riedijk SR, Aalten P, et al.: Impact of behavioural problems on spousal caregivers: A comparion between alzheimer's disease and frontotemporal dementia. Dement Geriatr Cogn Disord 2006;22:35-41.
16. Bakker C, de Vugt ME, van Vliet D, et al.: Predictors of the time to institutionalization in young-versus late-onset dementia: results from the needs in young onset dementia (NeedYD) study. Journal of the American Medical Directors Association 2012;14: 248–253.
17. Drijgers RL, Aalten P, Winogrodzka A, Verhey FR, Leentjens AF: Pharmacological treatment of apathy in neurodegenerative diseases: a systematic review. Dementia and Geriatric Cognitive Disorders 2009;28(1): 13-22.
18. Lane-Brown AT, Tate RL: Apathy after acquired brain impairment: a systematic review of non-pharmacological interventions. Neuropsychological Rehabilitation 2009; 19(4):481-516.
19. Treusch Y, Majic T, Page J, et al.: Apathy in nursing home residents with dementia: results from a cluster-randomized controlled trial. European Psychiatry 2015;30(2): 251-257.
20. Brodaty H, Burns K: Nonpharmacological management of apathy in dementia: a systematic review. American Journal of Geriatric Psychiatry 2012;20(7):549-564.
21. Leontjevas R, Teerenstra S, Smalbrugge M, et al.: More insight into the concept of apathy: a multidisciplinary depression management program has different effects on depressive symptoms and apathy in nursing homes. International Psychogeriatrics 2013; 25(12):1941-1952.
22. Buettner LL, Fitzsimmons S, Atav S, Sink K: Cognitive stimulation for apathy in probable early-stage Alzheimer's. Journal of Aging Research 2011;480890:1-6.
23. van Vliet D, Persoon A, Bakker C, et al.: Feeling useful and engaged in daily life: exploring the experiences of people with young-onset dementia. International Psychogeriatrics 2017;29(11):1889-1898.
24. de Vugt M, Dröes R: Social health in dementia. Towards a positive dementia discourse. Aging and Mental Health 2017;21(1):1-3.
25. Vernooij-Dassen M J, Jeon YH: Social health and dementia: the power of human capabilities. International Psychogeriatrics 2016;28(5):701-703.
26. Mariani E, Vernooij-Dassen M, Koopmans RTCM, Engels Y, Chattat R: Shared decision-making in dementia care planning: barriers and facilitators in two European countries. Aging & Mental Health 2017;21(1):31-39.
27. Garms-Homolova V, Notthoff N, Declercq A, et al.: Social and functional health of

home care clients with different levels of cognitive impairments. Aging & Mental Health 2016;21(1):18-23.

28. Lueken U, Völker SU, Schweiger E, Krusse A, Schröder J: Development of a short version of the Apathy Evaluation Scale specifically adapted for demented nursing home residents. American Journal of Geriatric Psychiatry 2007;15(5):376-385.

29. Archipel Zorggroep: Sociotherapeutische leefmilieus. 2016, Retrieved from https://www.archipelzorggroep.nl/_asset/_public/PDF/Folders-Brochures/Kennis-centrum/Sociotherapeutische-leefmilieus.pdf.

30. Stuurgroep jong dementerenden: Sociotherapeutische leefmilieus voor jong dementerenden. 2004, Retrieved from https://kcdementieopjongeleeftijd.nl/wpcontent/uploads/2016/04/Sociotherapeutische-leefmilieus-2007.pdf.

31. UKON: LIVE: Leefmilieus In Verpleeghuizen. Retrieved from https://www.ukonnetwerk.nl/LIVE.

32. Pieper MJC, van der Steen JT, Francke AL, et al.: Effects on pain of a stepwise multidisciplinary intervention (STA OP!) that targets pain and behavior in advanced dementia: A cluster randomized controlled trial. Palliative Medicine 2018;32(3):682 692.

33. Ruikes FGH, van Gaal BGI, Zuidema SU, et al.: The association between implementation and outcome of a complex care program for frail elderly people. Family Practice 2018;35(1):47-52.

34. Baum F, MacDougall C, Smith D: Participatory action research. Journal of Epidemiology and Community Health 2006;60(10):854-857.

35. Van Buul LW, Sikkens JJ, Agtmael MA, et al.: Participatory action research in antimicrobial stewardship: a novel approach to improving antimicrobial prescribing inhospitals and long-term care facilities. Journal of Antimicrobial Chemotherapy 2014;69:1734-1741.

36. Vilans: Psychofarmaca bewust gebruiken. Retrieved from https://www.vilans.nl/projecten/psychofarmaca-bewust-gebruiken.

37. Zorginstituut Nederland: Kwaliteitskaders verpleeghuiszorg. 2017, Retrieved from https://www.zorginstituutnederland.nl/publicaties/publicatie/2017/01/13/kwaliteitskader-verpleeghuiszorg.

38. Ministry of Health, Welfare and Sport: Radicale vernieuwing. Retrieved from: https://www.radicalevernieuwing.nl/.

39. Prins E, Hendriks A: Een kwestie van focussen: Effectief omgaan met jonge mensen met frontotemporale dementie. Denkbeeld 2017;6.

40. Zuidema SU, de Jonghe JF, Verhey FR, Koopmans RCTM: Psychotropic drug

prescription in nursing home patients with dementia: influence of environmental correlates and staff distress on physicians' prescription behavior. International Psychogeriatrics 2011;23:1632-1639.

41. van Duinen-van den IJssel JCM, Mulders AJMJ, Smalbrugge M, et al.: Nursing Staff Distress Associated With Neuropsychiatric Symptoms in Young-Onset Dementia and Late-Onset Dementia. Journal of the American Medical Directors Association 2017; Epub ahead of print.

42. Ballard C, Howard R: Neuroleptic drugs in dementia: benefits and harm. Nature Reviews Neuroscience 2006;7(6):492-500.

43. Schneider LS, Dagerman K, Insel PS: Efficacy and adverse effects of atypical antipsychotics for dementia: meta-analysis of randomized, placebo-controlled trials. American Journal of Geriatric Psychiatry 2006;14(3):191-210.


Family
I'm glad I
I love you
I wish I could remember
Pain
New challe
help
happiness
love
love life
how
Take care of the children
I forgot
I don't know
Golden years
enjoy
Good life
Work
learning
why
angry
I have
Friends
to grow
away from home
the beginning

Chapter 8

SUMMARY/SAMENVATTING
DANKWOORD
CURRICULUM VITAE

Summary

Neuropsychiatric symptoms (NPS), like aggression, apathy, hallucinations, and depression occur in almost all nursing home (NH) residents with young-onset dementia (YOD); defined as dementia with a symptom onset before 65 years. As in late-onset dementia (LOD), psychotropic drugs are often used in the treatment of NPS in NH residents with YOD. The prevalence rates of NPS and psychotropic drug use (PDU) seem higher compared to those in NH residents with LOD, but studies directly comparing NPS in heterogeneous samples of NH residents with YOD and LOD are still lacking. In NH residents with LOD, NPS and PDU are associated with a loss of quality of life of the NH resident. However, to our knowledge no studies on the influence of NPS and PDU on quality of life of NH residents with YOD have been conducted.

The high rates of NPS and PDU stresses the need for non-pharmacological interventions especially in the management of NPS in YOD. Therefore, in the Behavior and Evolution of Young ONset Dementia part 2 (BEYOND-II) study a multi-component intervention for the management of NPS in NH residents with YOD was developed and implemented in YOD special care units (SCUs). This thesis is part of the Beyond-II study and the methodology of the Beyond-II study is discussed in chapter 4. The general aim of this thesis is to provide knowledge to further improve specialized long-term care for people with YOD. This thesis focuses on consequences of NPS and PDU for the quality of NH residents with YOD and differences in NPS between NH residents with YOD and LOD. In addition, the implementation process and effects of the multi-component intervention for the management of NPS in YOD on the prevalence of NPS and PDU in YOD are evaluated.

In the introduction of this thesis (chapter 1) background information on YOD, the study rationale, and the research questions are described. In chapter 2, the determinants of quality of life of NH residents with YOD are explored. In addition, it is investigated if these determinants differed between dementia subtypes. Residents' quality of life is negatively associated with advanced dementia, PDU, agitation, aggression, depression, and apathy. In addition, aspects of quality of life differ by dementia subtype. Residents with FTD show less negative emotions, accept more help and experience better quality of relationships with professional caregivers, have a more positive self-image, feel more comfortable in the NH environment, and experience lower quality of social relationships compared to residents with Alzheimer and vascular/mixed dementia.

In chapter 3, the differences in NPS between heterogeneous samples of NH residents with YOD and LOD are investigated. In addition, it is explored if these possible

differences could be attributed to differences in dementia subtype, gender, psychotropic drug use, or dementia severity. Higher rates of apathy are found in NH residents with YOD compared to LOD. No differences in other NPS between YOD and LOD are found. Furthermore, higher levels of PDU in YOD compared to LOD are found, irrespective of the occurrence of NPS.

In order to interpret the effects of the intervention for the management of NPS specifically in YOD, information on validity and degree of implementation is important. Furthermore, implementation knowledge is important to optimize implementation strategies for future complex interventions in applied NH care. Therefore, in chapter 5, a process evaluation is performed. The process evaluation shows sufficient internal and external validity, allowing for further effect analyses of the intervention. Staff turnover and shortages, organizational changes, lack of involvement in the educational program, and overlap with current working methods are perceived as important barriers for implementation by the multidisciplinary teams. Facilitators that are mentioned involved: multidisciplinary collaboration, limited involvement in other projects, openness to change in working procedures, and the support of the ambassador and management. In none of the SCUs all steps of the intervention are completely carried out as planned. Recommendations for future implementation are integration of the intervention in the electronic health records, allowing for customization of the intervention to the context of a specific setting, and taking into account the aspect of readiness to change of users of the intervention in the development and implementation strategy.

In chapter 6, the effect of the multi-component intervention on the prevalence of NPS, with agitation and aggression in particular, as well as PDU in NH residents with YOD is compared to care as usual. No decrease in agitation and aggression, other NPS, or PDU is found after implementation of the intervention. Overlap between the intervention and working methods already used before implementation, might have diminished the intervention effect. In future research, more research on the specific needs and context of YOD SCUs during the development phase of an intervention is important to improved relevance and effectiveness of an intervention in this specific context.

In chapter 7, methodological considerations of this thesis are discussed. The findings are considered within the context of daily practice. In addition, recommendations for future research are addressed.

Samenvatting

We spreken van dementie op jonge leeftijd wanneer de eerste verschijnselen van de dementie voor het 65e levensjaar zijn aangevangen. Probleemgedrag, zoals agressie, angst, hallucinaties, apathie en depressie, komt bij bijna alle verpleeghuisbewoners met dementie op jonge leeftijd voor. Net als bij de behandeling van probleemgedrag bij oudere mensen met dementie, worden bij jonge mensen met dementie vaak psychofarmaca voorgeschreven. De prevalentie van probleemgedrag en psychofarmacagebruik bij verpleeghuisbewoners met dementie op jonge leeftijd lijkt hoger dan bij oudere verpleeghuisbewoners met dementie. Dit is echter nog niet eerder onderzocht in heterogene studiepopulaties van verpleeghuisbewoners met dementie op jonge en oudere leeftijd. Bij oudere verpleeghuisbewoners met dementie hangt de aanwezigheid van probleemgedrag en psychofarmacagebruik samen met een slechtere kwaliteit van leven. Er zijn nog geen studies gedaan naar de invloed probleemgedrag en psychofarmacagebruik op de kwaliteit van leven van verpleeghuisbewoners met dementie op jonge leeftijd.

De hoge prevalenties van probleemgedrag en psychofarmacagebruik bij verpleeghuisbewoners met dementie op jonge leeftijd benadrukken het belang van effectieve niet-medicamenteuze interventies voor probleemgedrag. Om deze reden is in de Behavior and Evolution of Young ONset Dementia part 2 (BEYOND-II) studie een interventie ontwikkeld speciaal voor de behandeling van probleemgedrag bij verpleeghuisbewoners met dementie op jonge leeftijd. Deze interventie is geïmplementeerd op gespecialiseerde verpleeghuisafdelingen voor mensen met dementie op jonge leeftijd verspreid over Nederland.

Dit proefschrift is onderdeel van de Beyond-II studie. De methodologie van deze studie wordt beschreven in hoofdstuk 4. De centrale doelstelling van dit proefschrift is het verbeteren van de gespecialiseerde verpleeghuiszorg voor jonge mensen met dementie. Het eerste deel van dit proefschrift richt zich op de consequenties van probleemgedrag en psychofarmacagebruik voor de kwaliteit van leven van verpleeghuisbewoners met dementie op jonge leeftijd en de verschillen in probleemgedrag tussen verpleeghuisbewoners met dementie op oudere en jongere leeftijd. In het tweede deel van dit proefschrift wordt het effect van de interventie voor probleemgedrag bij verpleeghuisbewoners met dementie op jonge leeftijd op de aanwezigheid van probleemgedrag en psychofarmacagebruik geëvalueerd.

In de introductie van dit proefschrift (hoofdstuk 1) wordt achtergrondinformatie over dementie op jonge leeftijd geven en worden de rationale en vraagstellingen van dit proefschrift beschreven. In hoofdstuk 2 worden determinanten van kwaliteit van leven van

verpleeghuisbewoners met dementie op jonge leeftijd onderzocht. Daarnaast wordt gekeken of deze determinanten verschillen tussen dementie subtypes. Verder gevorderde dementie, psychofarmacagebruik, agitatie, agressie, depressie en apathie zijn van negatieve invloed op kwaliteit van leven van verpleeghuisbewoners met dementie op jonge leeftijd. Daarnaast wordt er verschil gevonden op aspecten van kwaliteit van leven tussen dementie subtypes. Verpleeghuisbewoners met frontotemporale dementie laten minder negatieve emoties zien, zijn meer bereid om hulp te accepteren, ervaren een betere kwaliteit van de relaties met professionele zorgverleners, hebben een beter zelfbeeld en voelen zich meer op het gemak in de verpleeghuisomgeving in vergelijking met verpleeghuisbewoners met Alzheimer of vasculaire/gemengde dementie. Daarentegen ervaren verpleeghuisbewoners met frontotemporale dementie een lagere kwaliteit van sociale relaties.

In hoofdstuk 3 worden de verschillen in probleemgedrag tussen heterogene studiepopulaties van verpleeghuisbewoners met dementie op jonge en oudere leeftijd onderzocht. Apathie komt veel vaker voor bij verpleeghuisbewoners met dementie op jonge leeftijd. Er wordt geen verschil gevonden in de aanwezigheid van andere vormen van probleemgedrag. Toch wordt er wel meer psychofarmaca voorgeschreven bij verpleeghuis bewoners met dementie op jonge leeftijd.

In hoofdstuk 5 worden de resultaten van de procesevaluatie beschreven. Inzicht in validiteit en mate van implementatie is belangrijk om de effecten van de interventie te kunnen interpreteren. Daarnaast draagt implementatiekennis bij aan het verder optimaliseren van implementatiestrategieën in toekomstige implementatiestudies. Uit de procesevaluatie komt naar voren dat interne en externe validiteit voldoende zijn, waardoor effectanalyse mogelijk is. De mate van implementatie wisselt tussen verpleeghuisafdelingen en implementatie is in geen één verpleeghuisafdeling optimaal. Wisselingen in personeel, personeelstekorten, organisatorische veranderingen, beperkte betrokkenheid in het scholingsprogramma en overlap met huidige werkwijzen worden als belemmerend ervaren voor implementatie. Bevorderend voor implementatie zijn goede multidisciplinaire samenwerking, beperkte betrokkenheid in andere (onderzoeks)projecten, openheid tot verandering en ondersteuning van een ambassadeur en het management. Voor toekomstige implementatie wordt aangeraden om de interventie te integreren in het elektronisch cliëntendossier. Daarnaast wordt aangeraden om meer variatie in de uitvoer van de interventie toe te staan, zodat er ingespeeld kan worden op de specifieke omgeving van een verpleeghuis. Ook is het van belang om bij toekomstige implementatie de gereedheid tot verandering van gebruikers van de interventie mee te nemen in de ontwikkeling van de interventie en implementatiestrategie.

In hoofdstuk 6 wordt het effect van de interventie op de aanwezigheid van probleemgedrag, met in het bijzonder agitatie en agressie, en psychofarmacagebruik vergeleken met standaard dagelijkse zorg. Na implementatie van de interventie wordt geen vermindering van agitatie en agressie, andere vormen van probleemgedrag of psychofarmacagebruik gevonden. Een verklaring voor het uitblijven van effect kan zijn dat de verpleeghuisafdelingen voor mensen met dementie op jonge leeftijd al (gedeeltelijk) effectieve werkmethoden hadden voor het structureren van de behandeling van probleemgedrag bij verpleeghuisbewoners met dementie op jonge leeftijd voorafgaand aan implementatie van de interventie. Mogelijk dat overlap tussen de al bestaande werkmethoden en de interventie het interventie effect heeft verminderd. In toekomstige onderzoek is het van belang om tijdens de ontwikkeling van de interventie meer aandacht te hebben voor de specifieke behoeften en context van verpleeghuisafdelingen voor mensen met dementie op jonge leeftijd. Hierdoor kan de relevantie en effectiviteit van de interventie verbeterd worden.

Tenslotte worden in hoofdstuk 7 methodologische aspecten van de studie en implicaties van de bevindingen voor de klinische praktijk besproken. Daarnaast worden aanbevelingen voor toekomstig onderzoek gedaan.

Dankwoord

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Curriculum Vitae

Britt Appelhof werd op 27 november 1990 geboren in Geldrop. In 2009 behaalde zij haar Gymnasium diploma aan het Strabrecht College in Geldrop.

Vervolgens is zij Psychologie gaan studeren aan de Universiteit Utrecht. Ter afsluiting van de master Neuropsycholgie heeft zij onderzoek gedaan bij Korsakovcentrum Slingedael te Rotterdam. Tijdens haar gehele master is Britt werkzaam geweest bij Archipel Zorggroep: eerst als stagiaire, vervolgens als psychologisch medewerker. Na het behalen van haar masterdiploma is ze bij Archipel Zorggroep blijven werken als psycholoog.

In 2015 is ze gestart als promovenda op de Behavior and Evolution of Young ONset Dementia part 2 (BEYOND-II) studie bij de afdeling Eerstelijnsgeneeskunde van het Radboudumc. Deze studie heeft geresulteerd in dit proefschrift. Momenteel is Britt nog steeds werkzaam als psycholoog bij Archipel Zorggroep en werkt zij daarnaast als post-doc onderzoeker bij de afdeling Eerstelijnsgeneeskunde van het Radboudumc.

Thesis defenses from The Radboud Alzheimer Centre in Nijmegen (RAC)

Appelhof, B (2019). *The management of neuropsychiatric symptoms in people with young-onset dementia. Improving specialized long-term care.*

Ooms, S.J. (2018). Sleep well, age well? *Assessing sleep disruption as a player in Alzheimer's disease pathogenesis.*

Arnoldussen, I. A.C. (2018). *Adiposity and the Brain. The adiposity-brain-axis in mice and men*

Jong, D.L.K. de (2018). *Regulation of cerebral perfusion in Alzheimer's disease: from seconds to months.*

Donkers, H.W. (2018). *Social Participation Dilemma's in dementia.*

Richters, A. (2018). *Network-based care for people with dementia: a complex transition.*

Spek, K. van der (2018). *Appropriate psychotropic drug use in institutionalized people with dementia. The PROPER-study*

Wiesmann, M. (2017). *Vascular risk factors and Alzheimer's disease.*

Rijpma, A. (2017). *Multi-nutrient interventions and brain metabolism in Alzheimer's disease: a spectrum of effects.*

Elsen, G. van den (2016). *Tetrahydrocannabinol in the treatment of neuropsychiatric symptoms in dementia.*

Vermeij, A. (2016). *Cognitive plasticity in normal aging and mild cognitive impairment: Shedding light on prefrontal activation*.

Müller, M. (2016). *Footprints of Alzheimer's disease. Exploring proteins and microRNAs as biomarkers for differential diagnosis.*

Bruggink, K.A. (2016). *Amyloid-ß and amyloid associated proteins in the pathology and diagnosis of Alzheimer's disease.*

Aalbers, T. (2016). *eHealth in the primary prevention of cognitive decline; The Brain Aging Monitor study.*

Maaden, T. van der (2016). *Improving discomfort in nursing home residents with dementia and pneumonia. Development, implementation and evaluation of a practice guideline for optimal symptom relief.*

Millenaar, J. (2016). *Young onset dementia, towards a better understanding of care needs and experiences.*

Döpp, C.M.E. (2015). *Making the jump-The translation of research evidence into clinical occupational therapy practice.*

Herbert, M. (2014). *Facing uncertain diagnosis: the use of CSF biomarkers for the differential diagnosis of neurodegenerative diseases.*

Ven, G. van de (2014). *Effectiveness and costs of Dementia Care Mapping intervention in Dutch nursing homes*

Bakker, C. (2013). *Young onset dementia: care needs & service provision.*

Meeuwsen, E.J. (2013). *Towards efficient dementia care : a comparison of memory clinics and general practitioners.*

Spijker, G.J.A.A (2013). *Systematic care for caregivers of people with dementia in community mental health services.*

Janssen, D. (2013). *The role of nutrition in Alzheimer's disease : a study in transgenic mouse models for Alzheimer's disease and vascular disorders.*

Zerbi, V. (2013). *Impact of nutrition on brain structure and function : a magnetic resonance imaging approach in Alzheimer mouse models.*

Voight-Radloff, S. (2012). *Cross-national transfer of community occupational therapy in dementia.*

Spies, P.E. (2012). *The reflection of Alzheimer disease in CSF.*

Joosten-Weyn Banning, E.W.A. (2012). *Learning to live with Mild Cognitive Impairment: development and evaluation of a psychological intervention for patients with Mild Cognitive Impairment and their significant others.*

Vasse, E. (2012). *A stepwise process for developing and implementing quality indicators to improve psychosocial dementia care in European countries.*

Slats, D. (2012). *CSF biomarkers of Alzheimer's disease; serial sampling analysis and the study of circadian rhythmicity.*

Leontjevas, R. (2012). *Act in case of Depression! Validation and effectiveness of a multidisciplinary depression care program in nursing homes.*

Timmer, N.M. (2011). *The interaction of heparan sulfate proteoglycans with the amyloid b protein*

Schölzel-Dorenbos, C.J.M. (2011). *Quality of life in dementia: From concept to practice*

Bruinsma, I.B. (2011). *Amyloidogenic proteins in Alzheimer's disease and Parkinson's disease: interaction with chaperones and inflammation*

Perry, M. (2011). *Development and evaluation of a Dementia Training Programme for Primary care*

Derksen, E.W.C. (2011). *Diagnostic disclosure: a basic intervention in dementia care*

Wetzels, R.B. (2011). *Neuropsychiatric symptoms in institutionalized residents with dementia: Course and interplay with cognition,quality of life and psychotropic drug use.*

Dado- Van Beek, H.E.A. (2010). *The regulation of cerebral perfusion in patients with Alzheimer's disease*

Jong, D. de (2010). *Anti-inflammatory therapy and cerebrospinal fluid diagnosis in Alzheimer's disease*

Persoon, J.W.B. (2010). *Development and validation of the Nurses' Observation Scale for Cognitive Abilities – NOSCA*

Meulenbroek, O.V. (2010). *Neural correlates of episodic memory in healthy aging and Alzheimer's disease*

Zuidema, S.U. (2008). *Neuropsychiatric symptoms in Dutch nursing home patients with dementia*

Graff, M.J.L. (2008). *Effectiveness and efficiency of community occupational therapy for older people with dementia and the caregivers*

Claassen, J.A.H.R. (2008). *Cerebral hemodynamics in aging: the interplay between blood pressure, cerebral perfusion, and dementia*

Wilhelmus, M.M.M. (2006). *Small heat shock proteins and apolipoprotein E in Alzheimer's disease*

Van Horssen, J. (2005). *Heparan sulfate proteoglycans and vascular pathology in Alzheimer's disease*